BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 34, No. 12 December, 1959

Toxicity of Pesticides

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Perspective

Well-known poisons such as arsenic, lead, mercury, cyanide and nicotine have been used as pesticides for many years mainly in agriculture and food storage. Since 1945 many new compounds have been introduced for the purpose of killing a great variety of pests, and a steady stream of articles discussing in a general way the dangers that can accompany the use of these new pesticides has perhaps created a false impression of the scale upon which poisoning has occurred. SIMMONS and HAYES (1951) briefly reviewed the published figures on accidental poisoning and showed that the accident record from the new pesticides was no worse than that from the older materials and, when compared with other toxic hazards, accidents from pesticides were few. CONLEY (1958) shows that there has been no important change in the total deaths due to poisons in the U.S.A. in the 40 years from 1915. During this period the use of the newer pesticides has developed on a very large scale. In 1955 suicides slightly exceeded accidents from poisons, and pesticides were responsible for 6% and 5·4% respectively of deaths from these causes. As an occupational hazard for agricultural workers poisoning from pesticides makes an insignificant contribution. From 1951 to 1955 in Britain there was 1 death from pesticides among 140 deaths due to tractors, falls, the attacks of bulls and similar hazards, while only 0·2–0·7% of 25,000 accidents causing lost time were due to poisons (EDSON, 1957). METCALF (1957) points out that in California, where about 8 m. acres are treated annually with pesticides, these chemicals caused 5% of 14,000 disability work injuries. Of these cases over half were due to skin damage rather than general poisoning. In California in 1954 one insecticide, parathion, caused 85% of the cases of systemic poisoning attributed to pesticides. In one area of the U.S.A. pesticides had been blamed as a contributory cause of fungus infections, hay fever, asthma, sinusitis, gastro-intestinal upsets, dehydration, alkalosis, malnutrition, pneumonitis, cancer, poliomyelitis, arteriosclerosis, heart disease and insanity (HAYES, 1954). A careful survey of such an area where DDT had been extensively used for several years failed to show any evidence of changes in the incidence of disease judged by hospital records (FOWLER, 1953).

The persistent interest in possible health hazards from pesticides cannot be attributed to any obvious gross effects on the health of the communities in which they

are used or upon large numbers of those who use them. This interest in the toxic hazards from pesticides appears to persist for a variety of general reasons such as:—

1. The development of many new materials often extremely efficient at killing pests which may range from those that are virtually non-toxic such as the selective herbicides to the very poisonous insecticide parathion. Useful simple classifications of common pesticides are given by EDSON (1955) and KLIMMER (1957–8), and some estimates of the lethal dose for man by DUBOIS (1958b).
2. A general increase in technology in agriculture with higher standards of production and quality has led to an ever greater use of increasing number of these materials. The demonstration that crippling human disease particularly in the less developed areas of the world may be eradicated or reduced by using pesticides has led to many entirely new applications of these effective materials.
3. Rising standards of occupational health demand that more attention be paid to the prevention of occupational poisoning.
4. The concern felt by many that the use of pesticides in agriculture may incidentally add "chemicals to food", and so add another threat to good health.

Occupational hygiene as it relates to agricultural or public health field operations is not yet a well-developed subject, but clearly it will eventually form the basis for a proper assessment of the real hazards offered by the application of pesticides.

This review will only consider selected topics and will be orientated towards the interests of those using pesticides in public health work rather than for agricultural operations. In many cases those working in the public health field may be called upon to use pesticides in areas more remote than farms and in communities where medical facilities are extremely limited. Attention will be paid to the information on how exposure occurs during the application of pesticides. Those pesticides that are either in widespread use or those that have been the cause of poisoning under some conditions will be considered. No attempt will be made to mention all the common pesticides. It should be remembered that many selective herbicides such as the chlorophenoxy acetic acids are very safe to use. Maleic hydrazide freed from the stigma of being a carcinogen (BARNES *et al.*, 1957) is virtually harmless. These and other non-toxic materials may find a use in public health work and are obviously to be preferred to toxic materials like DNOC or pentachlorophenol (see below) for controlling vegetation.

Exposure to Pesticides

Hazards from toxic chemicals in industry are assessed by discovering how the worker becomes exposed to them. This involves a study of the operations in which the chemicals are used, the quality and design of the equipment and the extent to which the workers' environment is contaminated. Obvious difficulties face anyone making similar studies of the operations in which pesticides are applied, but some useful information has been obtained.

Because most pesticides are applied as fine sprays or dusts in order to ensure their adequate distribution over crops or wall surfaces it has perhaps been reasonable to assume that the major route of entry of a toxic pesticide has been through the respiratory tract. On the basis of such an impression, gasproof, air-conditioned tractor cabs were used by one firm applying DNOC as a herbicide (HUNTER, 1950). Some of the earliest studies on exposure during the spraying of parathion centred on the measurement of the concentration in the air round sprays and dusting equipment used in orchards. (KAY *et al.*, 1952; BRAID, WINDISH & ROSS, 1955). The concentrations round the operators were mostly less than 1 μgm./litre. BATCHELOR & WALKER (1954) and BATCHELOR, WALKER & ELLIOTT (1956) carried out more detailed studies on the actual exposure of operators applying parathion and DNOC in orchards. They measured the amounts of pesticide falling on various parts of the body surface and the quantities held up on filters fitted to respirators. Their data demonstrated beyond question that in this type of operation it is the skin and not the respiratory tract that is most severely exposed to the pesticide during its application. With parathion only 0·06 mgm. was inhaled each hour while 55·8 mgm. fell on the exposed parts of the body during the same period. In normal working clothes these were the face, hands, forearms, neck and upper front of the chest. Exactly similar data were obtained when the contamination from DNOC applied in a similar operation was measured. The authors pointed out that an exposure to parathion of the magnitude they observed might have been expected to produce symptoms of poisoning if man were as sensitive to parathion as are laboratory animals. Although blood cholinesterase estimations were not made on these men they showed no symptoms of parathion poisoning. BATCHELOR & WALKER (1954) thought this might be due to several factors such as the prolonged duration of the exposure before a toxic dose level was acquired, giving time for detoxication. There would also be some removal by washing, which the men did several times during the day, and possibly more protection from clothing than the authors allowed in their calculations. In the case of the men applying DNOC blood levels up to 10 μgm./ml. were observed (BATCHELOR, WALKER & ELLIOTT, 1956).

BORDAS *et al.* (1958) found concentrations of 0·5–1·35 mgm./m.^{3} of methyl parathion and malathion in the atmosphere during orchard and beet spraying. In Rumania, WASSERMANN and his colleagues (1959a) have found atmospheric levels around 1 mgm./m.^{3} in orchards during winter spraying with DNOC and similar levels for DDT and BHC in forest spraying (WASSERMANN *et al.*, 1959b). On the other hand the DNOC falling on the body of the orchard workers was equivalent to a dose of 6·6 mgm./kgm. in an 8-hour day.

A study of the hazards from tractor-driven sprays putting up the comparatively non-toxic insecticides has been made by CULVER, CAPLAN and BATCHELOR (1956). The average air concentration round the jeep driver was 2–4 mgm./m.^{3} and 0·5 mgm./m.^{3} 10–25 yards from the spray boom. The authors calculate that in 4 weeks at 40 hours' work per week the *total* intake by the respiratory route would be 5–11 mgm./kgm., while during the same period 17–45 mgm./kgm. would be deposited on the skin of the operators.

There seems no doubt at all that the skin is the main site of contamination by pesticides during a variety of outdoor application techniques and it must therefore be considered to be the main portal of entry of a pesticide into the body of the operator.

Indoor applications of pesticides have also been studied. In horticulture it is usual to put up pesticides in greenhouses as fumes, smokes or fine aerosols. Either full protective clothing with respirators is worn during the application (CULVER, KINOSIAN, THIELEN and GRAUL, 1958) or the operator leaves the greenhouse in front of the cloud he is putting up (HUGHES & READ, 1959). Both these groups of investigators found that workers handling the treated plants in the greenhouse got a little pesticide on the skin but in quantities that could not be considered harmful. Why the workers studied by CULVER *et al.* (1958) showed some fall in blood cholinesterase was not ascertained. Methyl demeton sprayed in a greenhouse did not raise the atmospheric level above 3·5 mgm./m.^{3} (KLIMMER & PFAFF, 1958). Much public health work with insecticides involves indoor spraying to put deposits on walls. The preparations are usually water suspensions of wettable powders. Despite the closed environment, measurements by WOLFE, WALKER, ELLIOTT and DURHAM (1959) during the application of a typical DDT wettable powder show that while only 7·1 mgm. per hour of spraying was inhaled, 1755 mgm. fell in the same period on the skin of the face, head, neck, arms and hands. A man spraying 4 hours out of an 8-hour day in an open-neck, short-sleeve shirt without hat or gloves would receive a dose of 105 mgm./kgm. on his skin. The spray pressure, type of surface and temperature also had some effect on the amount of spray deposited on the operator. While most of those who apply pesticides will distribute the diluted material some will have to handle the concentrates and these must obviously present a much greater potential hazard to the careless worker. SUMERFORD *et al.* (1953) demonstrated this in a study of different groups of people connected with the commercial spraying of orchards with parathion. Only among the mixing plant personnel was there evidence of undue exposure represented by a significant fall in cholinesterase levels (see below) of the group during the spraying season. Full-time and part-time applicators were not so affected. PETTY *et al.* (1959) found no fall even in mixers using parathion and methyl parathion in Louisiana. The danger from concentrates is illustrated by experience with DNOC. The 8 fatal cases of poisoning in Britain were in men handling 50% DNOC diluted to 0·5–0·8% for application (BIDSTRUP & PAYNE, 1951). American orchard workers used a 19% concentrate diluted to 0·02% and no evidence of intoxication appeared (BATCHELOR, WALKER & ELLIOTT, 1956). In locust control work 20% DNOC in oil is sprayed. RAINEY (1958), summarizing experience with 70,000 gallons of this DNOC solution applied by aircraft, notes that a blood level exceeding 20 μgm./ml. was only observed in 19 of 234 tests and of these 15 were in staff loading the aircraft. The others were aircraft cleaners and truck drivers. RAINEY also records that a highly concentrated (85%) diazinon preparation used against locusts was safely handled in field trials with only one instance of a possible slight depression of blood cholinesterase.

Aircraft spraying presents special hazards to the flying crew. The need for properly designed equipment has been stressed (INGRAM, 1951). A special type of hazard for the pilot has been indicated by UPHOLT *et al.* (1956) who point out that a splash in *one* eye by an anticholinesterase insecticide which has a direct miotic effect (*e.g.* TEPP) may produce more serious difficulties in judging distances than a bilateral miosis. The contamination of those on the ground during aerial spraying has been measured by CAPLAN, CULVER and THIELEN (1956) when malathion was being used for outdoor mosquito control. Discharged at the rate of 0·46 lb per acre from a height of 70 ft. the atmospheric concentration was less than 0·1 mgm./m.^{3} outdoors or in buildings in the area. Total exposure of a man working outdoors during the spraying amounted to 3·5 mgm. while he inhaled less than 0·2 mgm. The observations mean that materials of a toxicity considerably greater than malathion could be safely applied this way over inhabited areas for insect control.

The health of those living in areas of intensive air and ground application of pesticides in orchards and cotton fields has been carefully assessed and no evidence found that such people have undergone any significant exposure to the pesticides being used (SUMERFORD *et al.*, 1953; FOWLER, 1953; QUINBY, WALKER & DURHAM, 1958; HAYES DIXON, BATCHELOR & UPHOLT, 1957). The inhabitants of houses treated with insecticides might theoretically be exposed to the active ingredient emanating from the sprayed surfaces. Most treatments of this type are designed for long-term effects so that loss by vaporization must inevitably be small. MALINA, KEARNY & POLEN (1959) analysed the air in houses treated for termite control with chlordane. Using a technique able to measure down to 0·005 p.p.m. they only found chlordane twice in 12 analyses and each was below 0·05 p.p.m. The hazards from contact with sprayed crops may be more serious. Parathion has been responsible for a number of outbreaks of mild poisoning among those picking, cultivating, thinning or respraying treated crops (QUINBY & LEMMON, 1958). The authors concluded that the parathion had been picked up on the skin and the inhalation of vapour in dense vines, for example, was not likely to be the source of the intoxication.

Protection

The evidence just summarized clearly points the way to the correct methods for the adequate protection of those applying pesticides. Gases, volatile materials or fine aerosols used in closed atmospheres obviously demand the use of a suitable respirator. However, under the conditions in which by far the greatest quantities of pesticides are applied in agriculture or public health work it is the skin that must be protected. In mixing and dilution of concentrates the hands are most exposed so that rubber gloves should be worn. Though the protection they give may not be absolute since some of the solvents such as xylene used in the concentrates can penetrate rubber, the speed with which splashes of a concentrate of a moderately toxic material like chlordane can produce fatal poisoning (DERBES, DENT, FORREST & JOHNSON, 1955) indicate the need for protection of the hands. Carelessly used, even the heaviest gloves will give only limited protection because the insides readily

become contaminated if the technique of removing and replacing gloves during work is not good (CULVER, CAPLAN & BATCHELOR, 1956).

The possibility of safer formulations to reduce the hazards from concentrates has been discussed by HAYES and PEARCE (1953), and DEICHMANN, BROWN & DOWNING (1952) claimed that the penetration of the skin by one insecticide was reduced by using a special emulsifier in the concentrates. Although possibilities may exist of increasing safety by modifying formulation it is the exact composition of the latter which will determine the adhesion, spreading capacity, phytotoxicity and price of the preparation hence its value as a pesticide.

Cotton clothing affords an adequate protection for the skin against wettable powder, as shown by WOLFE *et al.* (1959) in their study of 5% DDT sprayed indoors. FLETCHER, PRESS & WILSON (1959), using similar experimental techniques, found that 0·5% dieldrin applied in a malaria control programme contaminated the men to the extent that they received a dose of 1·8 mgm./kgm. each day. The unprotected DDT spraymen received over 105 mgm./kgm. Regular washing of cotton protective clothing is recommended. Though soap and water failed to remove all of an insoluble material like dieldrin, FLETCHER *et al.* (1959) showed that no transfer to the skin followed the wearing of such washed clothes. Nevertheless they recommended an occasional wash in petrol, which dissolves most of these materials. The WHO Study Group on Toxic Hazards of Pesticides to Man (1957) outline the protection needed by those applying pesticides indoors and emphasize the need for protection of the head and shoulders. WOLFE *et al.* (1959) have given details of the design of suitable protection for the head, shoulders and face. A visor of some transparent material will protect the skin of the face but is liable to become opaque from the spray deposited on it. WOLFE and his colleagues found that a plastic gauze (20 x 20 mesh) allowed good visibility, afforded adequate protection from droplets, did not get occluded and was comfortable to wear. Protection is only likely to be effective if the organisation of those applying a toxic material is satisfactory. FLETCHER *et al.* (1959) describe how dieldrin has been safely applied and give full details of the operations of their team. Unfortunately similar studies are not available on workers in teams where poisoning has taken place.

Summaries of the safe handling of pesticides have been given by many people. EDSON (1956) summarizes some 20 important points and includes an outline of the Poisonous Substances Regulations as they apply to agriculture in the United Kingdom. COOK (1956) in another review refers to such points as the hazards of casually transporting drums of concentrate in ordinary automobiles, and this is also referred to by ASHDOWN, DAHMS, RIDGWAY and STILES (1952).

Individual Insecticides

DDT

For a material with such a considerable biological activity which has been used on a wide scale with virtually no safety precautions for 15 years, DDT has a remarkable record of harmlessness. No authentic case of occupational poisoning by DDT has been recorded even among the workers in public health programmes where contact has been most extensive, most prolonged and probably most intimate. This record should be borne in mind by anyone considering the replacement of DDT by insecticides about which less is known or experience has been less fortunate. There is a large literature on DDT but it is not yet possible to say just where it exerts its poisonous action in the mammalian body or with what biochemical or physiological mechanisms it interferes. The whole subject has recently been most comprehensively reviewed by HAYES (1959b) in several fully documented chapters. It will suffice here to take a few points only and discuss them briefly. A comparison between the action of DDT on mammals and insects has been given and the many points of similarity underlined (WINTERINGHAM & BARNES, 1955). DDT is safe to handle because it only penetrates mammalian skin with great difficulty, it acts slowly and its poisonous effects are fully reversible. No pathological lesions have been described except moderate liver cell injury when lethal doses have been given to animals. Human poisoning by DDT has been described by several authors (*e.g.* GARRETT, 1947; HSIEH, 1954) and has always been the result of ingestion of DDT usually finding its way accidentally into food. The description of several episodes gives a distinctive and consistent picture. Early nausea and vomiting are usual. Headache, weakness, dizziness, numbness, paraesthesia, incoordination and tremor come on within a few hours and may persist for several days but recovery is complete. The toxic dose for man by mouth is around 10–20 mgm./kgm. (the LD50 for animals is about 250 mgm./kgm.) but a man has survived a dose of 285 mgm./kgm. (GARRETT, 1947). An interesting case is reported by ONIFER and WHISNANT (1957) of a butcher who had a vaporizer working continuously in a poorly ventilated room in which he spent most of the day. The vaporizer was charged with DDT and BHC and was not thermostatically controlled. Paraesthesia, tremors, fatigue and unsteadiness resembling the signs of DDT poisoning were observed. The symptoms cleared up completely when the man was removed from further exposure. Although this man probably only received a comparatively small dose of DDT he almost certainly received it by inhalation and not from skin contact. What part, if any, the simultaneous exposure to BHC may have played is not known.

The literature is scatterd with accounts of cases said to be the result of poisoning by DDT. Such accounts have been adequately criticised by HAYES (1959b). It would perhaps not be unfair to say that all these accounts have one or more of the following features:—

(a) The poisonous effects consist of a well-known clinical syndrome for which, among any group of hospital patients, it is often impossible to give a cause, *e.g.* peripheral neuritis, agranulocytosis, purpura.

(b) There is a complete absence of any of the authentic symptoms and signs of DDT poisoning so well described in the papers referred to above.

(c) A complete diversity of the clinical pictures of the various cases recorded.

(d) The victim has often had an absolutely minimal exposure to DDT, either at work or from its use in the home.

(e) There has been a failure to consider critically the features of the illness and the possibility of other causes.

(f) The authors lack any first-hand knowledge of DDT as a poison for man or in the laboratory. This is often evident from their ignorance of the literature or their highly selective and ill-balanced assessments of previous observations.

Unfortunately, inaccurate and inadequate accounts tend to be referred to again and again by successive authors. As HEYROTH (1952) pointed out in discussing the report of a doubtful case of insecticidal poisoning, care should be taken to see that titles of papers do not have "a degree of finality not apparent in the authors' own comments."

If DDT is capable of causing human illness other than specific poisoning, those in charge of malaria spray teams are the people who will detect these cases for they are in touch with the most exposed groups of workers. A careful study of 40 men exposed for ½–8 years, in DDT formulating plants where no protective clothing was worn, revealed no evidence of disease attributable to the exposure nor did there appear to be any unusual rate of turn-over of workers in these particular factories (ORTELEE, 1958). Controlled administration of DDT to volunteers in doses of 3·5 mgm. and 35 mgm. per man per day produced no symptoms even when dosing was continued for 18 months. The level of DDT in the fat rose to over 200 p.p.m. in the men on the highest dose (HAYES, DURHAM & CUETO, 1956). This compares with the average level of 4·9 p.p.m. in the general population of the United States. The DDT in those not occupationally exposed comes from food—mainly fat of animal origin (HAYES, QUINBY, WALKER, ELLIOTT and UPHOLT, 1958). No account of alleged DDT poisoning has yet been accompanied by a figure for the DDT level in the fat.

There is no simple clinical or biochemical test that can be used to detect exposure to and absorption of DDT. Biopsy and the analysis of body fat for DDT is not a practical procedure. On the other hand the estimation of the main metabolite of DDT, namely DDA (dichloro-di-phenyl acetic acid) in the urine is feasible in a good laboratory and reflects the uptake of DDT (HAYES, DURHAM & CUETO, 1956). However, in the absence of any evidence of illness that can be attributed to exposure to DDT there is no incentive to organise tests of this kind on workers who use this insecticide. A number of compounds chemically related to DDT are effective insecticides though less widely used.

Methoxychlor

Methoxychlor is virtually non toxic to mammals by mouth or when applied to the skin, though by intravenous injection it is as toxic as DDT (personal observation). It is metabolized very rapidly by the liver and the breakdown products appear in the bile of rats (WEIKEL, 1956, 1957).

DDD

DDD is also almost non-toxic to mammals but it has an unusual effect on dogs, causing an atrophy of their adrenal cortex (NELSON & WOODARD, 1949). Attempts to use DDD for the therapeutic reduction of adrenal cortical activity have been unsuccessful (SHEEHAN, SUMMERS & NICHOLS, 1953; ZIMMERMANN *et al.*, 1956), indicating that man, like the rat, is not sensitive to this action of DDD (STONER, 1953).

BHC

The original preparation contained the alpha, beta, gamma and delta isomers of which the gamma isomer is insecticidally active and is now available alone as lindane. Lindane is a little more toxic than BHC probably because in the mixed isomers the sedative effects of the beta and delta isomers counteract the convulsive action of the gamma isomer. Like DDT, BHC has an excellent record of widespread use without evidence of occupational poisoning. There is a single record of a woman who had a fit the day after helping her husband to spray calves and cattle; some of the calves died (HERBERG & WRIGHT, 1955). Accidental poisoning has occurred under a variety of circumstances including the administration of BHC as a vermifuge. GRAEVE and HERRNRING (1949) describe one man who felt ill and another who had a fit after 45 mgm. BHC. KLOSA (1950) on the other hand recorded only mild symptoms such as burning of the tongue after 40 mgm. daily for 10 days. Increasing the dose to 90 mgm. produced only mild symptoms. SCHMIEDEBERG and WASSERBURGER (1953) recorded fits and loss of consciousness in a man taking 1,000 mgm. Recovery in these and other episodes of acute poisoning was rapid, which is consistent with the evidence that BHC is rapidly metabolized (ASPEREN and OPPENOORTH, 1954). Other cases of poisoning have arisen from the misuse of BHC powder to control parasites and domestic pests. DANOPOULOS, MELISSINOS and KATSAS (1953) recorded 79 such cases with 6 deaths. The signs of poisoning—prolonged in some cases—were lassitude, spasms, paresis, ataxia, tremor and mental confusion. Probably because of its widespread use rather like DDT, BHC has been debited with a number of illnesses the reports of which bear all the characteristics of those recorded above for cases of alleged DDT poisoning. Clinical tests for exposure to BHC are not described. As with DDT there is no incentive to explore possibilities. Phenobarbitone will control convulsions (BUCK, PFANNEMÜLLER, 1957; NICHOLLS, 1958).

Dieldrin and Related Insecticides

Aldrin, dieldrin, endrin and isodrin are four closely related chlorinated methano-naphthalenes very active as insecticides. Their chemical structure is clearly depicted in the paper of TREON and CLEVELAND (1955). Dieldrin has been responsible for a great many cases of poisoning among those applying it in public health programmes in many different parts of the world (HAYES, 1957). Aldrin, dieldrin and endrin have also been used extensively in agriculture but there are no reports of poisoning during their use on crops. There is one account of men poisoned by aldrin in a formulating plant (NELSON, 1953). As aldrin appears to be oxidized to dieldrin within the animal body (BANN, DECINO, EARLE & SUN, 1956) and poisoning by endrin (DAVIES & LEWIS, 1956) seems to be very similar to that produced by dieldrin, it will be convenient to discuss dieldrin as a type substance in this group. Chlordane is chemically related to dieldrin and though

less toxic its action is similar (STOHLMAN, THORP & SMITH, 1950; AMBROSE *et al.*, 1953). It has had a limited use in public health work and more considerable use in agriculture. Occupational poisoning has not been described but accidental poisoning has occurred (see below).

Dieldrin as an acute poison has a violent convulsive action in all species studied (TREON & CLEVELAND, 1955). Pharmacological studies have confirmed that the threshold for central reflexes is decreased and the effects on cats and rabbits are counteracted by barbiturates (GOWDEY *et al.*, 1954). However, there is little support from other evidence for the views of these authors that the action of dieldrin is similar to that of eserine and possibly related to an effect on cholinesterase. Although there may be points of resemblance between the action of DDT (BROMILEY & BARD, 1949) and dieldrin on the decerebrate cat there is little if any similarity between their action as poisons in man. Considering its widespread use and interest as a toxic material, it is surprising how little experimental work has been reported on dieldrin and related compounds. The literature is fragmentary compared with that on the organo-phosphorus compounds. Nothing is known of its metabolism except that there is some tendency for dieldrin to be stored in fat (BANN *et al.*, 1956). No suggestion can be made for any biochemical basis for the toxic effects produced by dieldrin. On one important point the laboratory study of the toxicity of dieldrin does help to explain the features of dieldrin poisoning described later. Dieldrin, whether applied as a powder or in a solvent, penetrates the skin of animals very readily so that the toxic dose by repeated application to the skin is very similar to that for dieldrin given by mouth (TREON & CLEVELAND, 1955; HAYES, FERGUSON & CASS, 1951). As discussed in an earlier part of this review, the skin appears to be the main site of contamination for a man applying pesticides under the usual conditions either indoors or outdoors. DDT and BHC have been applied safely for years in malaria control work. The toxic dose of DDT or BHC when applied to the skin of animals is 2 or more grammes per kgm. whereas dieldrin can kill rats and rabbits at less than 300 mgm./kgm. (HAYES, FERGUSON & CASS, 1951; TREON & CLEVELAND, 1955). It is utterly misleading to claim that "the fact that aldrin and dieldrin are innately more toxic to animals than DDT need not be of concern . . . because (they) have a very high toxicity to insects and consequently they are generally applied at only a fraction of the dosage or concentration at which DDT is normally used" (*Shell Technical Bulletin* ADB 421/Da 10). Such a view disregards the fact that the original concentrated preparation may well be the same though it may be diluted more before application. As noted earlier it is the manipulation of the concentrated pesticides that is often the hazardous part of the operation of applying pesticides. Such a view also ignores any differences there may be in the toxic properties of two pesticides such as the readiness with which they penetrate the skin.

Dieldrin has been used safely for many agricultural purposes but wherever it has been extensively used for spraying houses in insect vector control programmes poisoning has occurred (HAYES, 1959a). On a small scale well trained operators have applied dieldrin safely for this purpose (FLETCHER, PRESS & WILSON, 1959). These authors discuss the reasons for their safety record when compared with the less fortunate experience of others. The concentration of dieldrin sprayed was low (1·1–0·55%) compared with the concentration of 1·25–2·5% sprayed in areas where casualties occurred. The hours of work were shorter than in Venezuela and the standards of hygiene were higher than in most other areas. However, HAYES (1959a) points out that the numbers exposed in the spraying operations described by FLETCHER *et al.* (1959) are very small compared, for example, to those at risk in Venezuela so that an incidence of poisoning of, say, 10% could not have produced casualties in the group studies by FLETCHER *et al.*, purely by chance.

An accessible first-hand account of dieldrin poisoning is that of PATEL & RAO (1958) but the most detailed reports of the largest number of cases come from Venezuela (BLÁZQUEZ & BIANCHINI, 1956; 1957a,b; CARRILLO, 1956; WINTHROP & FELICE, 1957). BLÁZQUEZ & BIANCHINI, (1957a) describe 3 stages of intoxication among the spraymen:—

(1) Headache, blurred vision and incoordination.
(2) Myoclonic spasms and falls sometimes without loss of consciousness.
(3) Epileptiform attacks.

The spasms and fits may come on unexpectedly either during work or at any other time, either when active or even in bed at night (PATEL & RAO, 1958). There is no "aura" and apart from headache and blurring of vision in some cases there may be no preceding symptoms of sufficient severity to have caused the poisoned man to complain. However, WINTHROP & FELICE (1957) showed that in men who were spraying dieldrin and examined carefully, compared with men not exposed to dieldrin, there was increased frequency of such symptoms as: headache, blurred vision, vertigo, dizziness, disturbance of sleep and muscle twitching. The signs of poisoning are consistent with what is known of the pharmacological action of dieldrin. No deaths have been recorded in the literature from dieldrin poisoning though HAYES (1957) refers to a single fatal case in a sprayman. Nor have persistent neurological sequelae—paralysis, ataxia, tremors etc.—been described in any of the recorded cases of poisoning.

Clinically, dieldrin poisoning has two features not readily explained on existing knowledge of its toxic properties. A long period of exposure is usual before the symptoms of acute dieldrin poisoning appear in spraymen. PATEL and RAO (1958) had one case after only 60 days of contact, but in Venezuela BLÁZQUEZ and BIANCHINI (1957a) found 4 months to be the minimum exposure period before poisoning appeared. PATEL and RAO (1958) suggest that this may be evidence of the development of some form of hypersensitivity to dieldrin but there is no confirmatory evidence yet available for such an explanation of this delayed response. Again, the first signs of poisoning may appear after exposure has ceased, or recur up to 100 days after removal of the patient from working with dieldrin (HAYES, 1957). Further experimental

work is needed to provide an explanation for these observations. The late recurrence of symptoms makes it impossible to recommend a safe period after which a poisoned individual may resume work with dieldrin (HAYES, 1957).

There are no tests available which will detect or measure the absorption of dieldrin and so provide warning of dangerous exposure. CARRILLO and BLÁZQUEZ (1955) described a test in which *Rhodnius* larvae were fed on dogs that had been dosed with dieldrin; the subsequent death of the larvae indicated the presence of dieldrin in the blood. This test has been recommended as an aid to diagnosis of suspected dieldrin intoxication in man (BLÁZQUEZ & BIANCHINI, 1957b). WINTHROP and FELICE (1957) found that direct blood dieldrin estimations were no value in determining whether or not exposure had taken place.

Barbiturates are effective in treating the convulsions in dieldrin poisoning in man (BLÁZQUEZ & BIANCHINI, 1957a) as they are in aldrin poisoning (SPIOTTA, 1951).

Prevention of poisoning must lie in adequate training to avoid gross over-exposure such as will occur if dieldrin powder is carried in the bare hands (PATEL & RAO, 1958). The workers in Venezuela abandoned the precautions suggested because they did not believe the poisoning would occur—"it had never happened with DDT" (CARRILLO, 1956). It is not reasonable to expect spraymen automatically to accept the fact that dieldrin is different from DDT; they must be educated to handle it carefully (*WHO Technical Report* Ser. No. 114). WINTHROP and FELICE (1957) recommend protective measures that would undoubtedly make it safe to apply dieldrin or indeed almost anything, but experience seems to show that hard work in hot climates will not be done in full protective clothing. WOLFE *et al.* (1959) have illustrated how the exposure of the face, head and shoulders may be simply controlled for indoor spraying. If facilities for good general hygiene—washing of both the sprayman and his clothes—are not available it is not safe to use dieldrin (HAYES, 1959a). It is not really possible to name any one factor as being responsible for dieldrin poisoning among spraymen. As HAYES (1959a) points out, the men inevitably become contaminated during application; even under the best conditions FLETCHER, PRESS and WILSON (1959) found that the men received a dose of 1·8 mgm./kgm. per day when using the most dilute spray (0·55%) of any employed in these operations. Stronger spray solutions, different spraying equipment, less skin protection, poor washing facilities and a generally careless technique, with longer hours of work over a more continuous period, will all add something to the risks.

It is not within the province of this review to discuss the relative merits of dieldrin, DDT and BHC as insecticides for mosquito control. Some pertinent information has been given by BURNETT (1957) from which it appears that dieldrin may have limited advantages under special conditions, for example where eradication is the aim. Whether or not the results of using dieldrin can justify the exposure of those who apply it to risks of an unpleasant and perhaps rather protracted, but not fatal, form of poisoning must be assessed by those responsible for recommending its use.

Organo-phosphorus insecticides

The best known insecticide in this group is parathion which was one of the earliest to be exploited and remains popular because it is effective and relatively cheap. Parathion has probably caused more accidents of all types than all other modern insecticides. The early development of parathion, coupled with the fact that the highly toxic potential war gases—sarin and tabun—are of the same family of toxic compounds has perhaps tended to overshadow the development of organo-phosphorus insecticides of very much lower mammalian toxicity. Malathion, for example, must rank among the least toxic pesticide of any type and there is an increasing number of organo-phosphorus insecticides of intermediate toxicity. It is impossible to discuss or even mention all the organo-phosphorus insecticides which have been developed and used. The review will be limited to parathion, diazinon and malathion, representing the severely toxic, moderately toxic and very mildly toxic groups of these insecticides. All have a potential or actual use in public health work. In considering other organo-phosphorus insecticides compounds it is possible to classify them into one of these three groups on the basis of their toxicity to mammals. In use they can then be treated accordingly.

Parathion has been widely used all over the world and from everywhere have come reports of poisoning—occupational, accidental, suicidal and homicidal. These reports are too numerous to list. In Japan, NAMBA and HIRAKI (1958) report that thousands of cases of poisoning have occurred but that at the same time the rice crop has been significantly improved by the use of parathion; most of the casualties in Japan are among the farmers. PRIBILLA (1955) in a very comprehensive review gives details of 34 fatal cases, mostly in Europe, of which only 7 were occupational.

Accidental deaths unconnected with the proper use of parathion will be considered later. MICHAUX, THIODET and DEYME (1954), RODIER (1955) and DELONS (1958) give accounts of occupational poisoning with some fatalities typical of those which occur when parathion is introduced into communities not properly adapted for the safe handling of dangerous pesticides. RATHUS and BOTTOMLEY (1958) and GILSENAN (1957) give accounts of typical types of carelessness leading to death in users of parathion who should have known better.

Although it is so toxic, parathion has been and continues to be widely used in safety by those who respect its potential dangers. In some cases little protective clothing is worn because of the heat, but good general hygiene will prevent poisoning from the inevitable skin contamination discussed above. In public health work parathion is valuable for indoor use for killing flies resistant to DDT and related insecticides. KILPATRICK and SCHOOF (1956) have described the efficacy of cotton cords soaked in parathion solution and suspended in rooms for controlling flies, and GLÖMME and SWENSSON (1958) have demonstrated the safety of such preparations in that they do not significantly contaminate the atmosphere. Parathion has been sprayed in large barrack rooms without the use of respirators (STEINIGER, 1951) for the control of bugs, but it has been pointed

out that the hazards facing those who made such occasional applications cannot be compared with those facing teams having to carry out such continued applications as would be needed were parathion to be used in work such as malaria control (*WHO Technical Report Ser.* No. 114, 1956).

Methyl parathion has been widely used in some areas in place of parathion (PETTY *et al.*, 1959). Although it is somewhat less toxic than parathion to mammals, DEICHMANN, PUGLIESE and CASSIDY (1952) rightly emphasize that "this compound and its formulations still represent highly toxic preparations". One possible safety factor in considering any di-methoxy phosphate *vis-à-vis* its di-ethoxy analogue is that cholinesterase inhibited by the dimethoxy compound is more rapidly reversed by natural hydrolysis (ALDRIDGE & DAVISON, 1953); *persistent* exposure of cholinesterase to a di-methoxy inhibitor, however, will more readily lead to a truly irreversible inhibition (ALDRIDGE, 1957). At this stage inhibited cholinesterase is not amenable to the action of reversing agents (HOBBIGER, 1956).

Diazinon is an organo-phosphorus insecticide of intermediate toxicity to mammals (BRUCE, HOWARD & ELSEA, 1955) and, to judge from the report of a single unsuccessful attempt at suicide, also less toxic to man (BOCKEL, 1957). It has been widely used in public health work for the control of flies resistant to the action of DDT, and in some countries it has been sold for domestic use for the same purpose. Diazinon has also been used in agriculture. Serious cases of occupational poisoning have not been reported. FLORIS and COSSU (1955) reported 2 mild cases of poisoning among 20 men applying diazinon for fly and mosquito control. During a month of work all the men showed some fall in blood cholinesterase levels more or less proportional to the duration of their exposure. The men were reported to have worked in overalls, rubber boots and gloves and respirators. MOSNA and ALESSANDRINI (1954) reported falls in blood cholinesterase in workers who did not wear respirators when applying diazinon indoors. They concluded that diazinon could be safely used for indoor spraying if full precautions were observed. Whether or not the respiratory route is the most important in the case of diazinon spraying would need further evidence. BRUAUX (1957) reported observations on 36 men spraying diazinon out of doors for fly control 5 days a week all the year round for 2 years in the tropics. Falls in blood cholinesterase were noted and some were as low as 20% of normal values, but no symptoms of poisoning were reported and low levels returned to above normal within 1½ months of removing the men from exposure. RAINEY (1958) records the safe use in field trials of a highly concentrated (85%) diazinon preparation sprayed from aircraft to kill locust swarms.

Malathion, though an efficient insecticide is, under ordinary circumstances, of extremely low toxicity to mammals (HAZLETON & HOLLAND, 1953); a dose of 1–2 gm./kgm. is needed to kill rats and dogs. In man there have been reports of a 34-month-old baby (GOLDMAN & TEITEL, 1958), and a woman aged 35 (WALTERS, 1957) who survived and rapidly recovered from a dose of malathion taken by mouth, which was great enough to cause an initial loss of consciousness. However, malathion must not be regarded as being completely harmless. A mysterious illness in a 10-year-old child the day after a picnic was finally traced to the fact that "fly flakes" a preparation based on malathion, had been liberally scattered round a hut where the children played and ran barefoot. The flakes were still in the child's clothes next day. She rapidly recovered when the malathion contamination was removed (PARKER & CHATTIN, 1955). The comparative non-toxicity of malathion for mammals is probably related to the speed with which part of the molecule is hydrolysed in the liver (O'BRIEN, 1957). However, this detoxication mechanism may be upset by other esterase inhibitors which include some *but not all* of the other organo-phosphorus insecticides (FRAWLEY *et al.*, 1957; COOK, BLAKE & WILLIAMS, 1957; DUBOIS, 1958a). The significance for men of the potentiation of the toxicity of malathion by other organo-phosphates cannot yet be assessed but the possibilities of some risk should be considered if mixtures of organo-phosphates are used.

The safety for urban inhabitants of aeroplane application of malathion sprays has been demonstrated (CAPLAN, CULVER & THIELEN, 1956 see above) and GOLZ (1959) has shown that 84 exposures to malathion domestic aerosol in 42 days produced no lowering of blood cholinesterase in 10 subjects. This indicates that such preparations are safe at least as far as their insecticide content is concerned. BRUAUX (1957) used malathion for outdoor spraying in fly control and during a year's experience of continual use found no reduction of serum cholinesterase but a slight reduction in the red cell enzyme.

Control of hazards from organo-phosphorus insecticides

All these insecticides probably owe their toxic action to the accumulation of acetylcholine in the tissues which follows the inhibition of the enzyme cholinesterase which is normally present at the sites where acetylcholine is liberated. In many cases death is due to paralysis of the respiratory centre (de CANDOLE *et al.*, 1953) probably coupled with inefficient functioning of the respiratory muscles. Some very toxic organo-phosphorus compounds (HEATH & VANDEKAR, 1957) do not penetrate to the brain so that the latter mechanism alone, or other mechanisms, may sometimes be responsible for death.

It has long been recognized that the earliest evidence of exposure to an organo-phosphorus insecticide may be obtained by measuring levels of activity of blood cholinesterase. Significant falls of activity may be observed before any symptoms have appeared and when this happens poisoning may be prevented by withdrawing the exposed people from further contact or tightening up the precautionary measures for their protection. The widespread use of blood cholinesterase determinations, and the demand for methods that can be used, literally, in the field have resulted in the transformation of what was once a procedure used by the experimental biochemist to a simple, if less accurate, manoeuvre for the technician working, if necessary, in the open air. A detailed account of the electrometric method (MICHEL, 1949), the cholorimetric method

(LIMPEROS & RANTA, 1953), the field test based on this by DAVIES and NICHOLLS (1955) and the rapid field test of EDSON (1958b) will be found as an annexe to the paper by BARNES, HAYES and KAY (1957) together with references to earlier accounts. A modification of the field test of DAVIES and NICHOLLS (1955), which it is claimed is easier to read, is given by FLEISHER, WOODSON and SIMET (1956). GOLZ (1958) has described another variant.

Everyone who is responsible for the health of workers applying the moderately or severely toxic organo-phosphorus insecticides should arrange for periodical blood tests for cholinesterase activity to be taken and there is no technical reason why these should not be feasible under any conditions in which it is possible to apply pesticides at all. The simplest method used on a single occasion will be enough to determine whether an individual has suffered a severe depression of blood cholinesterase and is being, or in danger of becoming, seriously poisoned.

However, to follow trends and pick up the earliest deviations from normal in blood cholinesterase activity, account must be taken of the range of values found in normal populations (CALLAWAY, DAVIES & RUTLAND, 1951; WOLFSIE & WINTER, 1952; RIDER *et al.*, 1957) before the significance of the level in an individual can be assessed. The day-to-day value in healthy persons may vary from ± 13% for the red cell and ±20% for the plasma cholinesterase (FRYER, STEEL & WILLIAMS, 1955). Similar variations in a small factory population were noted by GAGE (1955). He suggests that if a person exposed to organo-phosphorus insecticide is found to have a cholinesterase activity of 50% or less of the average for the population he should forthwith be removed from further exposure. Levels of 50%–60% should act as an "alerting signal" for more care and the need for further tests.

WOLFSIE (1957) has reviewed his experience of 5,000 tests done over a period of 10 years and recommends that plasma and red cell determinations should be done separately in order to get the maximum amount of information from the test. The pre-exposure levels are also valuable. FRYER and WILLIAMS (1956) have given their experience in the control of agricultural workers applying organo-phosphorus insecticides. While pre-exposure values are always useful in increasing the sensitivity of the test as an indicator of early poisoning, it should be remembered that the facilities available to the industrial physician such as WOLFSIE (1957) will not be available to many in charge of public health programmes. They should not be deterred from using the simpler, cruder methods because they fall short of an ideal.

While the general surveys of SUMERFORD *et al.* (1953) indicated trends in one particular group of workers—*e.g.* the mixers of concentrates, using parathion—a survey of 245 farmers, pilots, mixers and others applying methyl parathion in Louisiana failed to disclose any depression of cholinesterase (PETTY, HEDWEG, REINHART, MOORE & DUNN, 1959). FRYER and WILLIAMS (1956) found 6 suspected cases of mild poisoning in a survey of 135 agricultural workers the majority of whom were handling parathion. All too frequently reports of occupational poisoning by organo-phosphorus insecticides include no record of any cholinesterase determination, indicating that no facilities were at hand. It seems likely that a team which is organized well enough to include regular blood cholinesterase determinations on its members will also have the rest of its routine well enough under control to reduce the risks of poisoning to a minimum.

Poisoning

The signs of acute poisoning by organo-phosphorus compounds have been described many times in the numerous accounts of cases of parathion poisoning. They have been summarized together with a few case histories from the literature by BARNES, HAYES and KAY (1957). Headache is common: this may be accompanied by miosis, but contracted pupils are not by any means always seen. Indeed dilatation of the pupils has been noted in authentic cases of parathion poisoning before atropine had been given (DIXON, 1957). Two important characteristics of parathion poisoning have repeatedly been stressed. The first serious symptoms may not develop until several hours after work has finished so the connexion between abdominal pain and occupational poisoning may not immediately be established (DELONS, 1958). Secondly a single dose of atropine will often cause a striking but only temporary relief of symptoms.

Repeated exposure to organo-phosphorus compounds by teams of men working in a spraying season may produce lowering of the blood cholinesterase and some mild symptoms. These have been studied by SUMERFORD *et al.*, 1953 and HAYES, DIXON, BATCHELOR and UPHOLT (1957). The latter report observations in over 500 people during 3 seasons. They list selected symptoms with the incidence among different groups of workers who had varying degrees of exposure. Their list of symptoms includes: headache, nausea, fatigue, tightness of chest, abdominal pain, vomiting, loss of appetite, sweating, disturbance of vision, miosis, insomnia. They conclude that miosis together with 3 or more of the selected symptoms given above is strong evidence of mild clinical poisoning. This occurred much more frequently in the exposed groups (such as mixers and full time applicators) during the spraying season. The authors point out that this type of poisoning from long-continued exposure was never serious or fatal. Serious poisoning was always associated with "brief, massive exposure and gross carelessness".

In a little-known paper HOLMES and GAON (1956) summarize their observations on 600 cases of poisoning from anticholinesterase agents which included war gases such as sarin, as well as insecticides. There are no details of how these men came to be exposed. One table shows that of 169 cases with a reduction of red cell cholinesterase of only 10% (*i.e.* still almost normal), 82% complained of tightness of the chest. This suggests exposure to vapour and as none of the commonly used insecticides are volatile the data implicate sarin as the major cause of poisoning in this series. A new feature in this important account is the evidence that repeated poisoning by these organo-phosphorus compounds could give rise to more persistent changes such as "dizziness, fatigability, impaired taste, numbness, irritability and confusion".

The general features of the personality change were "forgetfulness and irritability". It is not possible to evaluate the significance of these observations in respect to the use of organo-phosphorus compounds in agriculture. Such possibilities must be borne in mind if men are employed all the year round applying toxic organo-phosphorus compounds in public health work as they now apply DDT or dieldrin.

The possibility that poisoning by organo-phosphorus insecticides may not be the result solely of effects on cholinesterase has been suggested by FRIBORSKA-WAELSCHOVA (1957) on the basis of a study of 11 cases. The careful surveys of HAYES *et al.* (1957) seem to exclude the likelihood of sequelae to mild exposure. Severe poisoning by any material is likely to induce long-standing subjective changes in some people. Whether or not organo-phosphorus insecticides are particularly prone to do this remains at present unproven. Serious persistent lesions from poisoning with these insecticides have been described for one material only—Mipafox (BIDSTRUP, BONNELL and BECKETT, 1953) —which is no longer marketed. Acute poisoning was followed by a neurological lesion clinically indistinguishable from ginger jake paralysis (tri-ortho cresyl phosphate (TOCP) poisoning). It was shown that Mipafox could produce a lesion in hens which was the same as that produced by TOCP (BARNES and DENZ, 1953). Many well-known organo-phosphorus insecticides were tested on hens but none was shown to be capable of producing this persistent type of paralysis (DURHAM, GAINES & HAYES, 1956). The isolated report by PETRY (1951) of polyneuritis in a man after exposure to parathion must have been a coincidence as no similar report has appeared despite hundreds of cases of parathion poisoning. Polyneuritis has been named as a sequel to exposure to several pesticides with a wide range of toxic properties and the case reports have the features described above (see under DDT). It is also impossible to attach much significance to the cases described by PETTY (1958).

The treatment of organo-phosphorus insecticide poisoning has long been based on the repeated administration of atropine in doses considerably greater than those usual for such procedures as preparations for surgical operations. 2 mgm. of atropine by intramuscular injection should be repeated every 30–40 minutes until the symptoms of poisoning such as colic or bronchial constriction are relieved or until mild atropine poisoning (dry mouth, warm skin and tachycardia) appear (BARNES, HAYES & KAY, 1957). The value and importance of early treatment with atropine combined with artificial respiration, where necessary, has been emphasized by FREEMAN and EPSTEIN (1955) in their analysis of 46 cases of severe poisoning with 23 deaths.

The injection of atropine is essentially symptomatic treatment as the drug counteracts the effects of an excess of acetyl choline at certain sites. Above all atropine protects the respiratory centre, interference with which is believed to be the cause of death in acute poisoning, but it does not prevent disturbances at the myoneural junction which interfere, among other things, with the function of the muscles of respiration. Hence the need for artificial respiration in some cases where atropine had been given (FREEMAN & EPSTEIN, 1955).

Arising from a study of the mechanism of the inhibition of cholinesterase by organo-phosphates has come the promise of a more specific therapy in anticholinesterase poisoning. The work has been conveniently reviewed and summarized by DAVIES and GREEN (1959). In the presence of certain reactive chemical groups such as hydroxylamines and oximes the inhibited enzyme can be induced to shed the phosphate moiety of the original toxic compound and become able once more to hydrolyse acetylcholine. The compound first shown to be therapeutically effective in animals poisoned by organo-phosphorus compounds was pyridine-2-aldoxime methiodide (P2-AM) (ASKEW, 1956; KEWITZ and WILSON, 1956). This compound has also proved effective in human poisoning by parathion. NAMBA and HIRAKI (1958) described 5 cases among many successfully treated by the intravenous injection of 1 gm. of P2-AM. ERDMANN, SAKAI and SCHELER (1958) and KARLOG, NIMB and POULSEN (1958) have described cases of attempted suicide successfully treated with P2-AM. In the case described by KARLOG *et al.* the patient developed signs of atropine poisoning from the large doses that he had received before the P2-AM was injected. With the restoration of cholinesterase activity acetylcholine will disappear and thus leave atropine to exert its effects unopposed. Although P2-AM has some therapeutic value when given alone, these therapeutic effects are greatly increased if atropine is given with it (ASKEW, 1957). Risk of atropine poisoning should not be considered a contra-indication to its early administration even if P2-AM may be available for use afterwards. The original P2-AM has been modified first by using the much more soluble methane sulphonate salt of pyridine-2-aldoxime (P2-S) (DAVIES, GREEN & WILLEY, 1959) and then by using coupled molecules such as N.N′ polymethylene bis (4-hydroxyiminomethyl-pyridinium bromide) (HOBBIGER & SADLER, 1959). Unfortunately P2-AM and related compounds are not effective against poisoning by all types of organo-phosphorus compounds. The well-known insecticide schradan being an example of one whose effects cannot be reversed (see DAVIES & GREEN, 1959).

Although it is unlikely that P2-AM would be given to anyone not already seriously poisoned there is reassuring evidence that P2-AM itself is not toxic to normal subjects should any error in diagnosis lead to its being given to a person not suffering from poisoning by an anticholinesterase (LADELL, 1958). Most of the P2-AM is excreted unchanged in the urine and the half life in the blood after a dose of 15 mgm./kgm. intravenously is 0·9 hour (JAGER, STAGG, GREEN & JAGER, 1958). There is every reason for ensuring that wherever men are exposed to parathion and related organo-phosphorus insecticides supplies of an appropriate reversing agent should be available as well as atropine. LADELL (1958) gives some advice on suitable methods for storing and dispensing P2-S.

DNOC

In the immediate post-war years di-nitro-*ortho* cresol (DNOC) was responsible for at least 8 deaths in

Britain when being used as a herbicide in the summer (BIDSTRUP & PAYNE, 1951). Scattered reports have come from elsewhere and DNOC and the related nitro-phenols have caused poisoning during manufacture (MALTER, 1949; SAITA, 1949). The toxic action of these nitrated phenols is well known. They stimulate metabolism by an effect of cellular respiration and in acute poisoning this may lead to death from respiratory and circulatory failure. In the subjects reported by BIDSTRUP and PAYNE (1951) who had been applying DNOC as a weedkiller in cereal crops, all except one had been working within 12 hours of death. This indicates the fulminating nature of poisoning by this type of compound. There is no specific therapy though the use of barbiturates should be avoided as they may enhance the toxic effects of DNOC (EDSON & CAREY, 1955).

There have been no accidents from DNOC in Britain in recent years. Not only are users more aware of the hazards as a result of legislation and publicity, but specific measures to detect absorption, by regular blood DNOC estimations, have been carried out among regular users. The technique for preventing DNOC poisoning is described by BIDSTRUP, BONNELL and HARVEY (1952) and HARVEY (1952). In locust control RAINEY (1958) has described the safe use of concentrated solutions of DNOC and prophylaxis has included regular blood DNOC determinations. STOTT (1956) described 2 cases of polyneuritis among these workers. The condition was very mild and rapidly cleared up after contact with DNOC had been stopped. The relation to exposure to DNOC remains uncertain.

Pentachlorophenol

Pentachlorophenol has a toxic action very similar to that of the dinitrophenols, and this is explained by the fact that they have a similar biochemical effect on cell metabolism (WEINBACH, 1954, 1956). Pentachlorophenol is used as a fungicide, herbicide and molluscicide. As a fungicide it may be used to dress timber by dipping cut planks in baths of it; deaths have been reported in France by TRUHAUT, L'EPEE and BOUSSEMART (1952) and in Sarawak by MENON (1958). As a herbicide it is used in pineapple cultivation and deaths from pentachlorophenol poisoning have been reported from Queensland (GORDON, 1956). Deaths have also been reported during the manufacture of pentachlorophenol (NOMURA, 1953). As with DNOC illness developed rapidly with all the evidence of an overstimulated metabolism—weakness and fatigue associated with profuse sweating followed by rapid collapse and death. In all the episodes the environmental temperature was high just as it was in the fatal DNOC cases in England. Few, if any, precautions were taken in handling the pentachlorophenol though as an industrial poison it is known as a skin irritant and the appropriate precautions are recommended. After 9 deaths had occurred in 18 months, among timber dressers safety precautions such as rotation of labour, the provision of protective clothing and washing facilities together with a reduction in the strength of the pentachlorophenol solution, MENON (1958) states that no further cases of poisoning occurred in the ensuing 18 months. As with DNOC there is no specific therapy, nor is there any test to detect absorption before intoxication supervenes. Pentachlorophenol has been used extensively as a molluscicide in bilharzia control work. Recently 2 fatal cases of poisoning have been described in men using the powder for this purpose (N. G. SHIRLEY, Private Communication). Its potentialities as a poison should therefore be borne in mind by anyone using it for this purpose.

Accidental Poisoning

There would be little profit in attempting to summarize or review the many reports of accidental poisoning due to pesticides that have not been directly related to exposure during their application. Such records are a memorial to human carelessness and do not differ from similar reports about many household chemicals, medicaments etc. that get into the wrong container, in the wrong place or into the wrong hands. For new chemicals, however, reports of such accidents and suicides do sometimes enable one to learn more about the lethal or toxic dose for man, the course of an attack of acute poisoning and any sequelae, and also the potentialities of a material for causing poisoning.

DDT. Poisoning in man has almost invariably been the result of DDT finding its way into food. A typical accident that poisoned 100 women is described by JUDE and GIRARD (1949) where flour was put into a container that had once held an insecticide powder. Only when the container was nearly empty did the flour contain enough DDT to poison those eating food made from it.

BHC. This has poisoned a number of children who found and chewed tablets containing it (SCHMIEDEBERG & WASSERBURGER, 1953; NICHOLLS, 1958) or swallowed an oily solution of lindane (BUCK & PFANNEMÜLLER, 1957). Despite severe convulsions, in several cases a complete and rapid recovery ensued. Barbiturates were given to the majority. Unfortunately no estimate of the doses received by the children can be made.

Aldrin. The clinical effects of a single dose of 25 mgm./kgm. taken by a 23-year-old male are well described by SPIOTTA (1951). In spite of intensive sedative treatment symptoms persisted for 12 days and EEG changes were present 46 days later. This is consistent with the fact that in occupational dieldrin poisoning symptoms may recur after exposure has ceased.

Endrin contaminated some flour in a sack which had been consigned in a railway wagon in which a leaking drum of endrin concentrate had previously travelled. About 100 people were poisoned from bread and cakes made from the flour and 30 of these had convulsions; the EEG readings taken in 7 cases were abnormal. Recovery here was rapid and complete (DAVIES & LEWIS, 1956). Unfortunately no estimation of the toxic dose could be made.

Chlordane is less toxic than aldrin to rats and also apparently to man. A girl swallowed an estimated dose of 32 mgm./kgm. in error for medicine. Symptoms developed 1½ hours later, culminating in convulsions 4 hours later. Thereafter recovery was rapid (DADEY & KAMMER, 1953). A child of 15 months was ill for 2 days after a dose estimated to be 10 mgm./kgm. of chlordane powder swallowed accidentally. The child

was given barbiturates which controlled the symptoms (LENSKY & EVANS, 1952). On the other hand a concentrate of chlordane spilt on the clothes and not immediately removed caused the death of a women aged 23 within an hour. Another woman aged 32 deliberately swallowed a dose of about 104 mgm./kgm. as a powder and died 9 days later in convulsions despite continued therapy (DERBES *et al.*, 1955).

Malathion had little effect on a baby given a bottle to play with by another child, the contents of which it sampled (GOLDMAN & TEITEL, 1958), and in a quite unusual case a woman survived the swallowing of a malathion concentrate taken as a cure for toothache (WALTERS, 1957).

Parathion provides an altogether different story. Its popularity as a suicide weapon in Germany, Denmark and Finland may be explained by its availability in small ampoules and also to the statements in early cases that death was rapid and painless (Dr. G. HECHT, personal communication). Of its rapidity the numerous reports of suicide bear adequate witness (see PRIBILLA, 1955). Children have been poisoned as a result of playing with "empty" containers carelessly left around (JOHNSON, 1953). Large-scale poisoning has resulted from the contamination of food. One incident involving 200 people is briefly described in a report of 22 children who were poisoned, of whom 8 died (WISHAHI *et al.*, 1958). In another incident over 1,000 people were poisoned, and more than 10% died, after parathion from a leaking container had contaminated food in a warehouse. From the report of the investigation into this incident it appears that the poisonous material was shipped and consequently treated as an innocuous material instead of being consigned properly (GOVERNMENT OF INDIA, MIN. OF HEALTH, *Report of the Kerala and Madras Food Poisoning Cases Enquiry Commission*, 1958). Self medication by rubbing parathion in the skin to kill parasites caused a serious but non-fatal poisoning (KOEFFLER, 1958). Ignorance led to the death of an Indian worker who tasted the contents of a bottle of parathion out of curiosity (ANANTASWAMY, GOWDA & RAO, 1957).

TEPP caused sudden death from a similar foolish act in America (KLENDSHOJ *et al.*, 1952) and near fatal poisoning of a man who refreshed himself with a melon from a field he had just sprayed (FAUST, 1949).

While it may be salutary to conclude with such reminders of the ability of some pesticides to kill or seriously poison people under some conditions there is also no doubt that with the simplest attention to the rules of good occupational hygiene, vast quantities of these materials can be safely used to the immense benefit of mankind.

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DATA ON PESTICIDES MENTIONED IN THE ARTICLE*

Common Name	*Chemical Name*	*Oral LD50 Rats (mgm./kgm.)*	*Percutaneous Single lethal dose Rabbits (mgm./kgm.)*
DDT	2,2-bis-(p chlorophenyl)-l,l,l,-trichloroethane	250	2800
DDD	2,2-bis-(p-chlorophenyl)-1,1-dichloroethane	2500	4000
Methoxychlor	2,2-bis-(p methoxyphenyl)-l,l,l,-trichloroethane	5000	>6000
BHC	Mixed stereo isomers of 1,2,3,4,5,6-hexachlorocyclohexane	1250	
Lindane	*Gamma* 1,2,3,4,5,6 hexachlorocyclohexane	125	4000
Chlordane	1,2,4,5,6,7,8 8-octachloro-2,3,3a,4,7,7a-hexahydro 4,7-methanoindene	250	800
Aldrin	1,2,3,4 10 10 hexachloro-1, 4 4a,5,8,8a-hexahydro 1,4,-endo, exo 5,8, dimethanonaphthalene	60	150
Dieldrin	1,2,3,4,10,10-hexachloro-6,7-epoxy-1, 4,4a 5,6,7,8,8a octahydro, 1-4 endo exo 5,8 dimethano naphthalene	50	250
Endrin	1,2,3,4, 10 10-hexachloro-6,-7-epoxy 1,4,4a 5,6,7,8, 8a octahydro-1, 4 endo endo 5,8-dimethano naphthalene	7♀ 40♂	125
Parathion	0,0,diethyl 0-p-nitrophenyl phosphorothioate	4	40
Methyl parathion	0,0,dimethyl 0-p-nitrophenyl phosphorothioate	15	300
Diazinon	0,0,diethyl-0-(2-isopropyl-6-methyl-4 pyrimidinyl) phosphorothioate	235	>4000
Malathion	0,0, dimethyl S-(1,2-dicarbo-ethoxy ethyl) phosphorodithioate	1200	>4000(rat)
DNOC	4,6 dinitro-*o* cresol	25	500(guineapig)
Pentachlorophenol	Pentachlorophenol	125	100
TEPP	Tetraethyl pyrophosphate	1·2	5

*Data from Handbook of Toxicology, Vol. III Insecticides W.B. Saunders. 1959, London and Philadelphia.

Public Health

OFFICIAL RECORDS W.H.O. No. 94. **First Report on the World Health Situation 1954–1956.** pp. viii + 392, 11 figs. 1959, May. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [17s. 6d.; $3.25; Sw.fr. 10.–.]

The Director General of the World Health Organization reports annually on the work of that body, but it was thought that each country should be given an opportunity of describing its own health situation. The story of their problems told by territories of differing economic and cultural backgrounds might be very useful to other governments discouraged by the size of the same problems facing them. The members of the Organization were, therefore, invited in 1956 to submit reports on the health situations in their territories during the period 1954–56. The individual reports of all these governments representing almost every country in the world, together with a general survey of the main subjects dealt with in the reports, makes up the volume.

A brief introduction is followed by Part I, consisting of nearly 100 pages divided into 7 chapters, which presents a general survey of the problems confronting the various countries and of the attempted solutions. A large variety of interesting subjects is discussed, only a few of which can be mentioned here. There is, for example, an interesting discussion of ways of measuring health, while as an indicator of positive health the proportion of people served by a piped water supply is suggested. It is estimated that during the last 12 years malaria morbidity and mortality throughout the world have been reduced to half of their previous figures but the remaining problem is immense, particularly in Africa. Though yaws still affects some 50 million people it is being eradicated but trachoma, and associated with it epidemics of bacterial conjunctivitis, remains a grave social problem. Changes in the incidence of chronic degenerative and malignant disease are occurring as a result of an increase in the proportion of elderly people in the population.

The role of various government departments is described, including town planning, the school health service and social welfare. It is pointed out that social security schemes depending on contributory insurance are of little value to ill-paid and irregularly employed casual labourers. The unity of medicine is stressed, and the important role of the hospital in restoring function and in rehabilitation. The influence of the hospital can be extended by means of associated clinics, often bedded, throughout the area served. The rural health unit and its subsidiary health stations are described and it is pointed out that these could be used to relieve the hospitals in fringe areas of towns. In discussing health education it is pointed out that this is a new field offering great scope, and that it should be associated at least temporarily with those services most likely to attract the people. It is interesting to note that emphasis is now being laid on the public health value of the supply of water in quantity rather than insistence on high quality.

There is an interesting discussion of domiciliary services, one development of which is the post-hospital treatment of chronic cases, which ensures better care and relieves hospital beds. The importance of public health training for all grades of medical personnel is pointed out, since social medical activities are now becoming part of their function and they are members of a health team. In discussing future developments it is stated that the modern concept of medicine is to improve the quality of life as well as to reduce sickness. With the control of communicable disease more attention is being given to educational services and health care. Preventive medicine is entering a new era in which international collaboration will prove invaluable, as it already has in the control of the quarantinable diseases and malaria.

Part II consists of the reports of the individual countries, grouped according to the 6 regions delineated by WHO and arranged in alphabetical order. At the beginning of each report is a brief factual account of the territory and then follows the account of its health problems and the activities of the health service.

The first number of a series is of particular interest and this series promises to be of great value. The reports are useful for reference purposes and give information as to what problems are being attacked, how, and with what success. Part I is of unusual value since it records briefly the basic experience of countries during the course of development and the lessons learned by them. It deals with the problems encountered throughout the whole range of social and economic development from the most primitive to the most advanced, and it is full of wisdom distilled from practical experience of surmounting difficulties. This report describes the path along which developments in health are proceeding and indicates the lines along which people should be thinking for the future.

T. H. Davey

SOUTH PACIFIC COMMISSION. Nouméa, New Caledonia, **Training for Health Education in the South Pacific. An Account of a Training Course in Health Education for South Pacific Health and Education Workers, sponsored jointly by the World Health Organization and the South Pacific Commission, held at Noumea, July/August, 1957** [BROWN, M. S.]. 1958, Oct., v + 72 mimeographed pp.

A previous study [this *Bulletin*, 1957, v. 32, 634] has indicated the part which health education might fulfil and the methods which it might employ in the islands of the South Pacific. The main recommendations concerned the holding of a training course for carefully selected people in the concepts, principles and methods of health education, the assignment of a health education specialist and the award of fellowships for study to suitable people from the islands. The present report takes up the recommendation about a training course and describes in full detail the way in which it has been implemented. Detailed planning culminated in the

assembly of a course including 50 staff and students of very varied origins. Of necessity the course was largely experimental, having as much the object of finding out what was the attitude of the attendants and what was their reaction to various forms of teaching as of imparting information in itself. It was devised as a practical course with as little didactic teaching as possible and much emphasis on practical types including various forms of study group, problem finding groups, special interest groups, deriving their authority from and reporting back to plenary meetings which constituted the source of authority. The topics studied included such matters as the health needs and problems of village life, who and what influenced the health of a village, how people grow up in different communities, how people learn and change their behaviour, methods and techniques in health education, and the planning and organization of health education. Much of this is illustrated by verbatim accounts of some passages in the discussion. A systematic evaluation at the end of the period showed that practically all the students underwent some basic change in outlook with regard to their approach to health education and techniques which should be followed, but that there was no great measure of imparting new knowledge or stores of information to them. This result coincided with the objectives for the course, which is considered to have been a success.

G. Macdonald

Maternal and Child Health

VERVOORN, J. D. **Obstetrics in Ahafo, Ghana.** *Trop. & Geograph. Med.* Amsterdam. 1958, Dec., v. 10, No. 4, 309–15.

The author writes from his experience as the medical officer of a mission hospital, where he saw 2,188 pregnant women. He gives a short account of some of the beliefs and customs of the African people of this part of Ghana, but comments that these are apparently weakening in the face of the growing appreciation of the benefits of western obstetrical methods. There has for many years been a thriving system for the training of midwives in the large hospitals of Accra and Kumasi, and in June 1956 there were 640 registered midwives.

Of the prenatal findings anaemia (with hookworm or *Ascaris* infection), malaria and deficiency of the B vitamins were prominent, and pelvic anomalies, possibly due to calcium deficiency, were occasionally observed. Habitual premature labour seems to be a feature, possibly related to anaemia, malaria, avitaminosis and perhaps a too low progesterone content. Treatment with iron, calcium, vitamin B complex, progesterone, and vitamin E is very successful in preventing premature labour. Patients are not given prophylactic drugs for malaria, but if they are suffering from it they are treated with chloroquine or amodiaquine.

Charles Wilcocks

BERFENSTAM, R. & BILLE, B. S. V. Rökning under graviditet och amningstid. Några synpunkter på en aktuell fråga. [**Tobacco Smoking during Pregnancy and Nursing. Some Aspects on a Question of Current Interest**] *Nordisk Med.* 1959, Aug. 27, v. 62, No. 35, 1294–6. [31 refs.]

"An inquiry among mothers showed that the rate of smoking, which before pregnancy was 36%, fell during pregnancy to 26% and during nursing to 19%. The corresponding figures for heavy smokers (more than 8 cigarettes per day) were 12, 6 and 4%.

"Published reports do not give any unequivocal answers to the question of the harmfulness of smoking during pregnancy and nursing, but on the basis of the measured concentrations of nicotine in breast-milk after heavy smoking amounts that are toxic to the child would be possible.

"Further research is necessary in order to find out, for instance, the role played in this connection by carbon monoxide, produced at tobacco smoking."

Vital Statistics and Epidemiology

HUGON, J. & LAMBILLON, J. Note sur l'évolution de la mortalité périnatale à Léopoldville. [**Course of Perinatal Mortality in Léopoldville, Belgian Congo**] *Ann. Soc. Belge de Méd. Trop.* 1959, Feb. 28, v. 39, No. 1, 59–68.

A very large improvement has been made in the perinatal mortality in Léopoldville: the rate per 1,000 was 32 in 1955–6 and only 14 in the first 8 months of 1958. Perinatal mortality in this study comprises stillbirths and deaths in the first 8 days of life. This fall in mortality is attributed to improvements in the obstetric service and to the employment of a full-time doctor. A unit for premature babies has been created and deaths from prematurity have fallen from 34% of the total deaths in 1955–6 to 14% in 1958. Forceps delivery and prolonged labour have been avoided if possible by either caesarian section, partial symphysiotomy and suction. A greater measure of supervision has been exercised over babies in their first days of life.

W. J. Martin

IPSEN, J., Jr. **Social Distance in Epidemiology. Age of Susceptible Siblings as the Determining Factor in Household Infectivity of Measles.** *Human Biol.* 1959, May, v. 31, No. 2, 162–79, 2 figs. [11 refs.]

A continuous chain of contact between infected and susceptible persons is the only process by which the reservoir of infection of certain contagious diseases, particularly those of the upper respiratory tract, is maintained. Thus contacts within households are particularly important in such infection chains and among the earliest measures of maximum infectivity of such diseases was the "secondary household attack rate", defined as the total number of cases in a household minus the number of primary cases divided by the total number of susceptibles in the household minus the number of primary cases. The use of this rate implies that maximum contact between infective and susceptible persons in a community occurs between members of the same household rather than between members of different households and that the same degree of contact obtains in all households. Although simple, this rate suffers from two important limitations; firstly it is not always known which members of a household are susceptible to a particular disease, and secondly, susceptibles may escape infection from a primary case but succumb to infection from a true secondary case of those diseases in which the period of infection is short. The second limitation tends to overstate secondary attack rates as defined above in communities where the families are large and consequently efforts have been made in the past to correct the rates for family size. The work done by GREENWOOD and later by BAILEY in this field is reviewed by the author who notes that the observed data relating to measles, which has been used often in such studies, are compatible with the theory that the risk of a susceptible child being infected by an infective sib depends upon environmental circumstances within the household. This implies differences in infectivity levels between households and, whatever may be the environmental factors concerned, the author suggests that the differences can be explained by taking into account the age composition of the children in a household when computing the secondary infection rates.

He demonstrates this suggestion by making a fresh analysis of the data reported in detail by WILSON *et al.*, (*Proc. Amer. Phil. Soc.*, 1939, v. 80, 357) relating to families consisting of two children with one primary case of measles. The statistical analysis of these data is given in detail and the following formula is derived:—

$$y = 0{\cdot}8979e^{-0{\cdot}001(x+z-15)^2 - 0{\cdot}005(x-z-4)^2}$$

in which y represents the probability of infection, and x and z the ages of the primary case and the susceptible child respectively. In these data the variation among the households can be reasonably explained as random deviations from the predictions from this relationship and the conclusion is drawn that the ages of the children are important factors in determining the chance of infection. Thus the risk of contact infections in households is unlikely to be uniform as it depends on the "social inter-relation between children as expressed by their relative age".

The absence of sufficiently detailed data relating to larger family units handicaps the author's development of the subject, but some attention is given to such families and he suggests that the above hypothesis explains the observed distributions of infective chains in 3-child and 4-child families which in earlier work have seemed to be incompatible with theories based on uniform risks of infection.

E. A. Cheeseman

REID, D. D. & FAIRBAIRN, A. S. **The Natural History of Chronic Bronchitis.** *Lancet.* 1958, May 31, 1147–52, 2 figs. [10 refs.]

The sickness records of 565 postmen who were prematurely retired because of chronic bronchitis, and of 45 who died from that disease, during 1950–4 are the main data used in this report. The subsequent fate of 500 of these men was obtained in 1957 so that in effect the results of following them up for varying periods from 3 to 7 years after retirement were available. For comparison "controls" were drawn at random from the records of postmen still in the service in such a way that each "bronchitic" was matched by a control of the same age, length of service and office. For 448 of the "bronchitics" and control pairs records referred back to a sufficiently early age for a comparison to be made of sickness absence at ages long before the "bronchitics" were invalided from the service.

At all age-groups the postmen ultimately retired because of bronchitis had more frequent and longer absences due to that disease than had their controls. The number of attacks per 1,000 man-years in the bronchitic group, with the attack rates for controls in brackets, were 122 (13) at ages 15–24 years, 145 (54) at 25–34, 254 (64) at 35–44, 736 (101) at 45–54 and 1,275 (129) at 55–59. In the same age-groups the average duration of an attack in days was successively 12·8 (2·8), 12·7 (7·3), 17·1 (11·2), 23·0 (14·9) and 40·6 (18·7). It is shown that these differences were in part due to the presence among the men ultimately retired because of bronchitis of a small group who were prone to absence from work, not only because of respiratory disease, but also because of asthma and other causes.

The frequency with which the men who were ultimately retired because of bronchitis were absent because of other illnesses is examined with particular reference to attack rates after the age of 45 years. Rates are shown separately for those who were still alive in 1957 (survivors) and those who had died by then (deaths); each group is compared with appropriate controls and in what follows the rates for controls are shown in brackets. The attack rates per 1,000 man-years for the "survivors" group were:—bronchitis 914 (115), upper respiratory disease 539 (321), asthma 56 (6), heart disease 28 (5), pneumonia 10 (2), pleurisy 17 (6), rheumatic disease 216 (122), gastro-intestinal disease 102 (75), skin disease 63 (37) and all other disease 915 (556). Corresponding rates for the "deaths" group were:—bronchitis 815 (82), upper respiratory disease 471 (359), asthma 56 (5), heart disease 54 (2), pneumonia 14 (2), pleurisy 17 (3), rheumatic disease 123 (122), gastro-intestinal disease 77 (56), skin disease 37 (54) and all other disease 731 (639). Thus after the age of 45 years there were 8–10 times as many attacks of bronchitis and

asthma and 3–5 times as much pneumonia and pleurisy among the men who were ultimately retired as bronchitic invalids as among those who were not, and those who died from bronchitis had experienced a very heavy attack rate from circulatory disease. The other non-respiratory diseases listed were slightly more frequent in the "survivors" group than in their controls but this was not a feature of the attack rates of the "deaths" group and their controls.

In all, 60 postmen who were retired because of bronchitis had a history of peptic ulceration compared with 46 of their controls. Only about 30 of the bronchitic group and 36 of the control group would have been expected to have such a history if the age specific incidence rates estimated in the Medical Research Council survey of occupational groups in 1951 had applied to the postmen.

Among the 500 postmen who were successfully followed up there were 113 deaths by 1957; when these were compared with the numbers expected from the appropriate age-mortality experience in England and Wales then, apart from the obviously excessive number of deaths due to bronchitis (51 observed and 2 expected) and other respiratory disease (11 observed and 1 expected), there was also a significant excess of deaths attributed to cancer of the lung (12 observed and 3 expected) and coronary disease (13 observed and 5 expected).

Attack rates from bronchitis among the postmen ultimately invalided because of this disease are tabulated for 4 sub-groups, I, II, III and IV. Group I included men working in areas with least air pollution and II to IV represents an increasing order of the frequency "of fairly dense and presumably polluted fog". At ages 25–34 years, the attack rates per 1,000 man-years were I 184, II 120, III 143 and IV 119; but at ages 45–54 and 55–59 a definite trend in the rates increasing from minima in group I to maxima in group IV was apparent. Thus at ages 45–54, the rates were I 568, II 579, III 748 and IV 967 attacks per 1,000 man-years and at ages 55–59 they were I 1,069, II 1,126, III 1,259 and IV 1,563 attacks per 1,000 man-years. After consideration of further analysis the authors conclude "Bronchitic postmen who had worked in the more fog-ridden parts of the United Kingdom had, after the age of 45, far more frequent absences from bronchitis, pleurisy, and pneumonia and circulatory disorders than bronchitic postmen from less polluted areas. The onset of bronchitic attacks was more closely related to fog frequency than to cold or humidity, and there were clear gradients between the less and more polluted areas in the short-term and long-term prognosis of the disease." *E. A. Cheeseman*

Communicable Diseases

For the bacteriology of these diseases see the Section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order: General; Hospital Cross Infection; Diphtheria, Whooping Cough, Streptococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis; Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Arthropod-borne Virus Infections; Enteric Fevers.

ANN. SOC. BELGE DE MÉD. TROP. 1958, Apr. 30, v. 38, No. 2, 241–385, illustrated. Symposium sur les maladies à virus en Afrique centrale. Stanleyville, 29 septembre–2 octobre 1957. **[Symposium on Virus Diseases in Central Africa. Stanleyville, 29th September–2nd October, 1957.]**

A symposium on virus diseases in Central Africa was held in 1957 on the occasion of the opening of the new laboratories. The opening address was given by P. BRUTSAERT on *The present situation of the problem of virus diseases in the Belgian Congo* (pp. 249–69). Smallpox is still a problem in spite of extensive vaccination, and 518 cases of variola major with 115 deaths and 5,699 cases of alastrim with 35 deaths were observed in 1955. The country has always been affected by influenza, and 92,071 cases were recorded in 1954 and 98,352 in 1955 among the African population. Yellow fever is still present in the area, and 35 cases have been diagnosed by post mortem examination since 1941. The history of the investigation of this disease was reviewed in the following paper by A. J. HADDOW, entitled *The present state of knowledge concerning yellow fever in Africa* (pp. 271–81). As a result of extensive field work carried out in the Bwamba area by workers at the East African Virus Research Institute at Entebbe it has been shown that yellow fever is an enzootic disease of monkeys transmitted by *Aëdes africanus*, human infection taking place when infected monkeys raid plantations and are bitten by *Aëdes simpsoni* which then bites man. In recent years it has been shown that bush-babies (*Galago* spp.) are susceptible to yellow fever, and it is now thought that in some areas these animals are the main reservoir of infection, which is probably transmitted by wingless arthropods in the nest. In West Africa the situation is different, and the disease chiefly occurs as the urban form in epidemics and is transmitted by *Aëdes aegypti*.

Poliomyelitis is discussed by J. P. DELVILLE and S. R. PATTYN (*Epidemiology of poliomyelitis in the Belgian Congo and Ruanda-Urundi. The present state of*

knowledge, pp. 283–92). The disease occurred in 1919–20 in the regions of Léopoldville and Stanleyville, and then virtually disappeared until 1934, since which time cases have been observed in the Belgian Congo every year, with a maximum of 1,447 in 1955 among a population of approximately 11,000,000. Among the Africans the disease mainly affected children up to 2 years of age. The disease is less frequently found in Ruanda-Urundi (population, 4,500,000) and tends to be sporadic: 17 to 21 cases were seen annually between 1952 and 1958. Virological investigations have only been carried out since 1954. 18 strains of virus were isolated during an epidemic in Elisabethville in 1954–5, all of which were of type 1, and this was also the prevailing type in other epidemics. The epidemiological conditions in Belgium were then discussed by E. NIHOUL, L. QUERSIN-THIRY, P. DE SOMER and A. PRINZIE (*Indications for anti-poliomyelitis vaccination in Belgium as a function of the immune state of the population*, pp. 293–302). From a consideration of the age-distribution of immunity they suggest that as the amount of poliomyelitis vaccine available is limited it should be given to children aged up to 1 year, and then to children aged 2 years, and so on, but if the available amount is unlimited, then all children aged up to 5 years should be vaccinated simultaneously. Conditions in Belgium were also described by P. RECHT (*The campaign against poliomyelitis in Belgium*, pp. 303–10) and P. DE SOMER (*Poliomyelitis vaccine in Belgium*, pp. 311–26). In the vaccine used in Belgium the Mahoney strain has been replaced by a non-pathogenic strain supplied by LÉPINE which possessed adequate antigenicity. Loss of antigenic material is inevitable during production and it is suggested that this loss could be reduced by altering the minimum requirements. A paper on *Vaccination by means of modified live viruses*, read by H. KOPROWSKI (pp. 327–46), is devoted entirely to a consideration of the production of attenuated strains of poliomyelitis virus.

After these interludes on European affairs the conference returned to its proper theme with a paper on *Problems of the arthropod-borne viruses in Africa*, by K. C. SMITHBURN (pp. 347–58). The viruses concerned are tabulated according to the parts of Africa in which they have been discovered and according to the haemagglutination groups of CASALS, and the part played in transmission by vectors and climatic factors is discussed.

The relationship of cirrhosis to previous infective hepatitis in the African is discussed by P. E. STEINER (*Some aspects of infectious hepatitis*, pp. 359–64), and the symposium ends with a paper by Lise QUERSIN-THIRY entitled *An in vivo study of the influence of tissue antisera on certain virus infections* (pp. 365–77), in which it is shown that the addition of specific cell antiserum to the homologous cultures in an appropriate dose will inhibit the multiplication of a number of viruses.

The concluding address on *The future of viruses in Central Africa* (pp. 379–85) was given by M. VAUCEL, who pointed out that viruses which are kept within bounds at the present time by immunological defences and delicate biological equilibrium may at some time in the future overcome their restraints and assume epidemic proportions among the African population. Other viruses have been discovered too recently for their importance as future sources of epidemics to have been ascertained.

D. J. Bauer

ANDERSON, K. *Pseudomonas pyocyanea* **disseminated from an Air-Cooling Apparatus.** *Med. J. Australia.* 1959, Apr. 18, v. 1, No. 16, 529.

The air cooling unit of a hospital operating theatre was found to be spraying *Pseudomonas pyocyanea* into the air; the cause was contamination of the cooling water. The regular addition of chlorhexidine to the water trough was recommended.

R. E. O. Williams

SAYERS, M. H. P., STEWART, R. C. & HOLT, P. R. **A Trial of Methods for Mass Inoculation.** *J. Roy. Army Med. Corps.* 1959, July, v. 105, No. 3, 127–31.

"The findings of Fleming & Ogilvie (1951) are confirmed and attention is drawn to the often neglected essential feature of this hot-oil sterilisation technique, namely that the thumb or finger *must control the plunger during injection, withdrawal and sterilisation.*

"Several modifications of this technique were tried but resulted in contamination of the syringe.

"A syringe incorporating a spring clip to stabilise the plunger and thus obviate the necessity for the operator to maintain pressure on the plunger was found to be ineffective after repeated trials.

"The syringe described by W. O. GROSS (1954) seems to offer an advance in mass inoculation technique in that it provides a more rapid method than others described. Again, however, with this syringe the thumb must control the plunger carefully during injection and withdrawal from the patient. Whether such control with a syringe of this bulk is practicable will have to be determined in a series of field trials by regimental medical officers. In our hands it proved possible to use the syringe in this fashion, and it may well prove to be a step forward in the provision of a safe mass inoculation technique."

GABRIELLI, G., SALETTI, M. & BRACCINI, L. Osservazioni sul valore immunizzante di un vaccino associato antitifo-paratifico-antidifterico a dose unica per la profilassi antitifoidea e per la vaccinazione antidifterica di richiamo. [**Observations on the Value of a Combined TAB and Diphtheria Vaccine in Enteric Prophylaxis and as a Diphtheria Booster Dose**] *Igiene Moderna.* 1959, v. 52, Nos. 3/4, 206–19. [23 refs.] English summary.

The authors studied the effect of a combined typhoid-paratyphoid-diphtheria vaccine containing 25 Lf doses of diphtheria toxoid adsorbed on 3·5 mgm. of $Al(OH)_3$, 1000 million *Salm. typhi* and 375 million each of *Salm. paratyphi A* and *B* per ml. The test was carried out on 100 boys between 2 and 14 years of age who had never been vaccinated against or suffered from enteric infection but who had been vaccinated against diphtheria. The changes produced were evaluated by the Schick reaction, by estimating the amount of diphtheria antitoxin,

of O, H, and Vi agglutinins, and by a study of the protective power of the serum against *Salm. typhi*. The presence of Vi antibodies was sought by putting up serum dilutions against red cells which had been sensitized by exposure to a Vi extract. The protective power of the serum against *Salm. typhi* was studied by a modified GRABAR and LE MINOR method [this *Bulletin*, 1952, v. 27, 367], in which a 1 in 10 dilution of serum is mixed with microbial suspensions containing 200, 2,000 and 20,000 bacteria per ml. and injected in the allantoic cavity of the developing chicken embryo.

None of the subjects of the test had originally any O, H, or Vi antibodies or any protective power against *Salm. typhi* in their sera. 6 months after vaccination O, H, and Vi antibodies against typhoid were sought in all, 42 reacting against H (mostly at 1/80 and 1/160), 35 against O (mostly at 1/40, 1/80 and 1/160), and 27 against Vi (15 at 1/10 and 12 at 1/20). 60 were examined for para-B O (7 positive), para-B H (1 positive) and para-A (13 positive—not stated if O or H). The protective power of the serum against *Salm. typhi* was tested in 12, in all of whom there was an increase, generally 10 to 20-fold, being positive even in 6 cases which showed no agglutinins.

14 of the boys had a positive Schick test initially which changed to negative. In 28 out of 30 in whom the diphtheria antitoxin content was estimated there was a 3–4 fold increase.

The authors think such a combined vaccine would be of special value to children going to holiday camps.

E. Agius

KUROKAWA, M. La vaccination antidiphtérique et l'état actuel de l'épidémie diphtérique au Japon. **[Diphtheria Inoculation and the Present State of Epidemic Diphtheria in Japan]** *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 168–80, 4 figs.

Compulsory diphtheria inoculation has been practised in Japan since 1948 but was held up during 1949 on account of a disastrous experience in the town of Kyoto where there were 606 very severe reactions and 68 deaths among 15,561 children inoculated, an accident which was traced to faulty inactivation of the toxin in the preparation issued. Since 1951, however, there has been a widespread inoculation of the population—rather over 40%. It is not clearly stated whether this is a percentage of the total population or of the children and adolescents.

Diphtheria morbidity which fluctuated from 30 to 50 per 100,000 of population in the first 40 years of the century, reached a peak about 1945, corresponding to the epidemic incidence of diphtheria in Europe. There was a marked fall in the incidence of diphtheria in the post-war period till 1952 when an unusually low level was recorded. There has, however, been a recent recrudescence so that between 1955 and 1957 the morbidity has risen to 11 per 100,000.

Rather imperfect records exist with regard to the types of diphtheria bacilli which have been active but an incidence of 60% *gravis* in malignant diphtheria was recorded in one infectious diseases hospital; this appears to have fallen away to an incident of 20% in the post-war period, with 50% of avirulent *gravis* type among carriers. By contrast, in the latest epidemic manifestation, there have been 70–80% of *gravis* strains over all cases and most of the strains have proved to be virulent.

The lack of investigations on the predominant types of diphtheria bacilli in the period intervening between the last war and the recent epidemic makes it impossible to say when this change took place.

An extensive examination of the Schick negative rate in the child population carried out in 1954 showed that only 20% were Schick negative. The duration of immunity following inoculation was considered to be 2–3 years. In view of all this, the recommendations at present operative in Japan are: combined diphtheria and whooping cough inoculation between the 3rd and 6th months, 3 injections at intervals of 3–4 weeks, a further injection between the 12th and the 18th months, another 6 months before starting school and a 4th vaccination 6 months before leaving the primary school.

J. W. McLeod

CALALB, G., SARAGEA, Alice, IEREMIA, T., MAXIMESCO, Paula, TUPA, Sanda, STĂNICĂ, Ecaterina, STOIAN, Cecilia, TAGA, Stefania & GARTNER, Magda. Contribution à l'étude des souches de *Corynebacterium diphtheriae* isolées dans deux foyers endémo-épidémiques: types et formes de variations en rapport avec les systèmes phago-bactériens spécifiques et les particularités endémo-épidémiques locales. **[Contribution to the Study of Local Strains of *C. diphtheriae* isolated from Two Endemo-Epidemic Foci; Types and Variants as related to Specific Phage-Bacterium Systems and to Local Endemo-Epidemic Peculiarities]** *Arch. Roumaines Path. Exper. et Microbiol.* 1959, Mar., v. 18, No. 1, 33–47. [33 refs.]

Antidiphtheria inoculation has been obligatory in Rumania since 1934 in which year, as before in 1897 and 1915, there was an epidemic wave of the incidence of this disease and it is suggested that the absence of a further epidemic wave since then may be explained by the prophylactic measures taken. There is, however, persistent diphtheria at a lower level; 5·7 cases and 0·4 deaths per 100,000 of population and a case mortality rate of 7·5% were registered in 1956.

In recent years, minor epidemics have occurred in towns designated S and C and the village F, and careful investigation of these has shown an interesting contrast. The variety of *Corynebacterium diphtheriae* which has accounted for the cases in S is described as being of *gravis* or *gravis-intermedius* type, susceptible to agglutination with sera prepared for such types, lysogenic and often resistant to phage lysis and mostly toxigenic both by *in vivo* and *in vitro* tests.

In the town C and in the village F the active strain is *mitis*. It is non-lysogenic but sensitive to phage lysis, it is insensitive to agglutination and about 50% of strains are toxigenic.

When a strain of *mitis* isolated from the village F was submitted to the action of various phages and colonies were selected from cultures of the strain so obtained it was found that not only were lysogenic and toxigenic strains isolated but the characters of the strain in culture might also be changed. These included variants of

gravis character with and without capacity to ferment starch.

[It is to be noted that in the original literature, which is not quoted, the term *C. diphtheriae gravis* is applied to a starch-fermenting strain with special growth characters in fluid and on solid media, whereas in this paper it appears to relate entirely to the appearance of colonies on the Gundel-Tietz medium.]

J. W. McLeod

BEALE, A. J. & CAMPBELL, W. **A Rapid Cytological Method for the Diagnosis of Measles.** *J. Clin. Path.* 1959, July, v. 12, No. 4, 335–7, 4 figs.

A method is described from Newcastle for the cytological diagnosis of measles in the prodromal period (up to 5 days before the rash), which although occasionally negative in subsequently proved cases did not give any false positive results. Material is obtained from the back of the nose by a polythene tube attached to a 20 ml. syringe. A small hole cut in the side of the tube, and closed with the finger during suction, allows more than one sucking operation without dislodging mucus already obtained.

Fresh smears may be fixed in 50–50 ether-alcohol and stained by the Papanicolaou method, or air-dried smears may be stained with Giemsa. Numerous syncytial giant-cells are found in a typical case; these are well illustrated by photomicrographs. Material from the front of the nasal fossa, or taken after the onset of the rash, shows large necrotic masses of cells, and diagnosis is then unreliable.

The method is particularly valuable in children's wards, and is reported to have been used with success at Ilesha, Nigeria.

Alan B. Raper

HENLE, W., CRAWFORD, Mary N., HENLE, Gertrude, FAZ TABIO, H., DEINHARDT, F., GUERRA CHABAU, A. & OLSHIN, I. J. **Studies on the Prevention of Mumps. VII. Evaluation of Dosage Schedules for Inactivated Mumps Vaccine.** *J. Immunology.* 1959, July, v. 83, No. 1, 17–28, 6 figs. [13 refs.]

A study has been made of the development of immunity in children inoculated with inactivated mumps vaccine given according to different dosage schedules. 60 children aged 1–5 years in an orphanage were divided into 3 groups and given 3 doses of vaccine at intervals of 1, 2 or 4 weeks respectively. The mean titres of complement-fixing and neutralizing antibodies in the 3 groups were similar; little effect was produced by the 3rd dose. In a second institution 119 children aged 1–5 years were vaccinated; only a small proportion developed neutralizing antibody after 1 or 2 doses of vaccine; after 3 doses antibody appeared in most cases but the titres were low. An epidemic of mumps occurred during the course of the investigation; the incidence of the disease among children who had received 2 or more doses of vaccine was 5·5%, compared with 31·8% in those given 1 dose and 30·2% among 189 susceptible children. In a third institution 55 susceptible children aged 6–12 months were studied. Neutralizing antibody appeared after 2 doses of vaccine; after 6 months the titres had fallen to low levels, but rose again to higher values after a booster injection; a similar response was also observed after a second booster injection given 6 months later.

D. J. Bauer

WILTERDINK, J. B., VERSTEEG, J. & KUIPER, A. Isolatie van $ECHO_9$-virus uit het speeksel van ontstoken speekselklieren. [**Isolation of $ECHO_9$ Virus from the Saliva of Inflamed Glands**] *Nederl. Tijdschr. v. Geneesk.* 1959, Sept. 12, v. 103, No. 37, 1847–9. [10 refs.]

The English summary appended to the paper is as follows:—

"$ECHO_9$ virus strains were isolated from the saliva of a mother and daughter, both with acute swelling of the salivary glands, and the tests for mumps virus were negative. Neutralizing and complement-fixing antibodies against $ECHO_9$ virus were demonstrated in serum taken some weeks after onset of the disease, although the titres were low. No serum was obtained in the acute phase, consequently no increase in antibody titre could be demonstrated. Enteroviruses might be aetiological factors in the syndrome of inflammation of the salivary glands."

CRONE, R. A. Vaccinia van de ogen. [**Vaccinia of the Eyes**] *Nederl. Tijdschr. v. Geneesk.* 1959, Mar. 28, v. 103, No. 13, 660–62, 1 fig. English summary (5 lines).

An account is given of 3 patients suffering from vaccinia infection of the eyes. (1) A woman aged 29 years who had never been vaccinated. 3 weeks after the vaccination of her daughter she developed conjunctivitis of the right eye with oedema of the eyelids and right half of the face; a number of typical vaccinia pustules appeared on the eyelids, and the preauricular lymph node was enlarged. Penicillin was given to prevent secondary infection and after 4 weeks recovery was complete except for symblepharon. (2) An unvaccinated woman aged 26, who was infected in similar circumstances. The patient was very ill, with a temperature of 39·2° C., enlargement of the preauricular lymph node, severe membranous conjunctivitis, and a typical vaccinia pustule in the left nostril. Recovery occurred after 3 weeks, with residual symblepharon and epiphora due to obliteration of the punctae. (3) A man who had been vaccinated in childhood developed membranous conjunctivitis of the right eye 6 weeks after the vaccination of his son. Vaccinia pustules appeared on the eyelid, followed by extensive keratitis with superficial ulceration and deep infiltration, associated with turbidity of the aqueous. The acute manifestations passed off after a few weeks, but the corneal infiltration persisted for 2 years and the patient was left with $\frac{1}{4}$ vision.

D. J. Bauer

SIFONTES, J. E. & MIRABAL FONT, E. **Complications of Smallpox Vaccination.** *Bol. Asoc. Med. de Puerto Rico.* 1959, June, v. 51, No. 6, 187–95, 2 figs. [11 refs.]

These notes are prompted by the observation of certain complications during a recent vaccination campaign in Puerto Rico. Pyogenic infection was the most

common. 2 cases of tetanus were seen. Lesions of secondary vaccination [accidental auto or hetero inoculations] are referred to and one case of "generalized vaccinia" is described in a child aged 1 year who never appeared seriously ill. Eczema vaccinatum is recognized as being particularly dangerous. Case histories, with photographs, are provided of 2 such patients who recovered after treatment, which included gamma globulin.

Progressive vaccinia, due to absence or deficiency of gamma globulin, is also recognized as a dangerous complication. If hyperimmune vaccinial globulin is not available, pooled gamma globulin should be used in larger doses (4 ml. per kgm.).

Only one case of possible post-vaccinial encephalitis was encountered, in a girl aged 3 years. This patient recovered, but with nervous sequelae, the outcome of which remains uncertain. *J. Pickford Marsden*

GRIST, N. R. & SOMMERVILLE, R. G. **Respiratory Virus Infections in the Glasgow Area.** *Brit. Med. J.* 1959, Apr. 4, 900–902. [15 refs.]

Between 1956 and 1958 virological investigations were carried out on 1,000 patients in the Glasgow area suffering from acute respiratory diseases. A diagnostic rise in adenovirus complement-fixing antibody was observed in 10 patients, 1 of whom had an illness resembling glandular fever. A rise in titre of complement-fixing antibody to the Sendai strain of influenza D was observed in 10 patients, 2 of whom also showed a rise in titre with mumps V antigen. An antibody response to A-prime influenza virus was observed in March–May 1957, and during the 2 waves of the Asian influenza epidemic which occurred in the autumn of 1957 and the first quarter of 1958 16 and 10 strains of virus were respectively isolated, none of which showed any signs of antigenic variation. 3 patients with encephalitis were observed in whom serological evidence of influenza infection was obtained.

[See also this *Bulletin*, 1957, v. 32, 405.]

D. J. Bauer

SIEGERT, R., FALKE, D., DIETRICH, F. & FRIOLET, B. Influenzavirus-Infektionen des Typ D/Sendai in Deutschland. **[Infections with Influenza Virus Type D/Sendai in Germany]** *Deut. med. Woch.* 1959, Apr. 3, v. 84, No. 14, 659–63, 706–7. [27 refs.]

In an investigation of sera taken from 541 patients during the influenza pandemic of 1957/58, 6 instances of infection with influenza virus of type D were observed. The case histories are given in detail, and the clinical aspects of the disease did not differ from those seen in infections with influenza viruses of other types. There was some association between influenza D infection and chronic respiratory diseases. In a note added in proof the authors mention a fatal case of meningoencephalitis which was apparently due to influenza D infection.

D. J. Bauer

TROTTER, Y., Jr., DUNN, F. L., DRACHMAN, R. H., HENDERSON, D. A., PIZZI, M. & LANGMUIR, A. D. **Asian Influenza in the United States, 1957–1958.** *Amer. J. Hyg.* 1959, July, v. 70, No. 1, 34–50, 8 figs. [17 refs.]

"The Asian influenza pandemic of 1957–1958 presented unusual opportunities for observation of the behavior of epidemic influenza in the United States. For the first time a new epidemic strain of virus was detected early enough to allow extensive preparations prior to the spread of the disease to this country from abroad." A considerable account is given in this paper of the elaborate preparatory measures which were taken. These included the development of a specific vaccine, organization of emergency health services and establishment of laboratory and epidemiological studies. The need for a "nationwide system of intelligence" led to the establishment of the Influenza Surveillance Unit, U.S. Public Health Service, in July, 1957, to collect, correlate and disseminate information about influenza derived from a number of different sources. Data on influenza were collected by means of a county reporting system established in 1957, by records of sickness absenteeism, by interviews in households organized by the National Health Survey established in 1957, by statistics of mortality from influenza and pneumonia obtained weekly from 108 large cities with an aggregate population of 50,000,000, and from other sources.

The epidemiological findings derived from study of the data are described in great detail with maps, figures and tables. The epidemic which began in the southern and coastal states and spread inward toward the central states started by first cases on June 2, 1957, rose to its peak in late October and then decreased as winter progressed. The magnitude of the epidemic is indicated by the estimate that in October and November, 1957, alone about 45,000,000 cases of influenza occurred. "Within individual cities students were first affected, followed in about 2 weeks by adults. The peak of deaths usually occurred after the peak of morbidity. There is evidence that this represents later involvement of old and debilitated persons."

The experience of influenza incidence and mortality from influenza and pneumonia in the United States is compared with that of England and some other countries. *M. E. Delafield*

WIDELOCK, D., KLEIN, Sarah, SIMONOVIC, Olga & PEIZER, Lenore R. **A Laboratory Analysis of the 1957–1958 Influenza Outbreak in New York City. II. A Seroepidemiological Study.** *Amer. J. Pub. Health.* 1959, July, v. 49, No. 7, 847–56, 5 figs. [13 refs.]

An extensive survey of haemagglutination-inhibiting (HI) antibodies for influenza viruses was conducted with 6,741 sera received from a syphilis serology laboratory over a period of 1 year, starting in September 1957. The results obtained with specimens collected between September 1957 and February 1958 have been previously published [WIDELOCK *et al.*, this *Bulletin*, 1958, v. 33, 928] and showed 2 marked rises in the percentage of sera containing Asian HI antibodies, each rise being

associated with an increase in the influenza-pneumonia mortality rate. The present paper extends the observations to September 1958. The percentage of sera with Asian HI antibody reached 70% at the end of the second epidemic wave and then declined to about 50% over the next 6 weeks, remaining at this level for the remaining 2 months covered by this study. Loss of antibody was observed mainly among the older age-groups and probably involved sera with low antibody levels at the end of the second wave. Evidence is presented suggesting an association between infection with Asian virus and antibody rises for FM1, PR8 and possibly Lee viruses.

H. G. Pereira

BLOM, P. S. & VAN LEEUWEN, P. Redding van een patiënt met fulminante influenza-viruspneumonie door snelle intraveneuze toediening van hydrocortison. [**Life-Saving Effect of rapidly administered intravenous Hydrocortisone in a Case of Fulminating Viral Influenza Pneumonia**] *Nederl. Tijdschr. v. Geneesk.* 1959, Jan. 17, v. 103, No. 3, 109–10. English summary (5 lines).

A man aged 30 years who had undergone valvulotomy for mitral stenosis 3 months previously developed an acute febrile illness with dyspnoea and oedema of the lungs which was first thought to be an attack of cardiac asthma. Treatment with digitalis, oxygen and antibiotics was unsuccessful and on the second day of illness the patient was in a moribund state. A diagnosis of influenzal pneumonia was then considered, and 100 mgm. of hydrocortisone in alcohol diluted with 100 cc. of 5% glucose solution was injected intravenously over a period of 2–3 minutes. The general condition improved rapidly and after 1 hour the pulmonary oedema had practically disappeared; pyrexia persisted for some time but responded to treatment with amidopyrine, and the patient was discharged in good health apart from the cardiac condition. Influenza virus of Asian type was isolated from the lung oedema fluid, and a rise in titre of inhibiting antibody could be demonstrated.

D. J. Bauer

WARBURTON, M. F., DUXBURY, A. E. & GREVILLE, R. W. **Antibody Response in Man to Two Doses of Polyvalent Influenza Virus Vaccine.** *Med. J. Australia.* 1959, June 13, v. 1, No. 24, 786–90, 4 figs. [21 refs.]

Antibody response to vaccination with polyvalent influenza vaccines was studied on the basis of haemagglutination-inhibition titres measured before and at varying times after vaccination of 2 human populations. The first population consisted of 104 adults and received 2 doses of a vaccine A containing each 200 chicken cell agglutinating (CCA) units of an Asian strain, 100 CCA units of an A-prime (A/WA) strain, 150 CCA of a recent B strain (B/Tas) and 100 CCA of influenza D (Sendai) virus. The interval between the 2 vaccine doses was 3 weeks and the volunteers were bled at the time of the first and second injections and then at weekly intervals for the next 4 weeks. The second population, consisting of 86 adults, received at 4 weeks' interval, 2 doses of a vaccine containing, in addition to the viruses included in vaccine A, the PR8 and swine strains of influenza A. The volunteers in this group were bled at the time of the 2 injections and again 2 weeks after the second injection. Blood samples were also obtained from all volunteers available 22 weeks after the second injection.

Antibody responses for all the virus strains included in the vaccines could be demonstrated by rises in mean antibody levels and by the proportion of subjects developing measurable haemagglutination-inhibition titres. The highest percentages of sera with presumably protective antibody levels were reached after the second vaccine dose, except in the case of PR8 antibodies which could be detected in 99% of sera tested after the first dose. Antibodies for all virus strains persisted at detectable level in a high percentage of volunteers tested 5 months after vaccination.

Findings on antibody responses to the Asian strain are presented in the following paper. *H. G. Pereira*

DUXBURY, A. E., WARBURTON, M. F. & GREVILLE, R. W. **Antibody Response to A/Asian Component of Polyvalent Influenza Virus Vaccine.** *Med. J. Australia.* 1959, June 13, v. 1, No. 24, 790–93, 3 figs. [10 refs.]

Rises in haemagglutination-inhibiting antibodies for Asian influenza virus were studied in the 2 volunteer populations vaccinated with polvalent influenza vaccines as described in the preceding paper [see above]. Both populations are considered to have been equally exposed to infection by Asian influenza virus during the year preceding the study. A large proportion (62%) of subjects included in population A had received a single dose of a monovalent Asian virus vaccine 6 to 7 months previously. Antibody for Asian influenza virus was detected in only 2 volunteers at the time of administration of the first dose of polyvalent vaccine. The percentages of volunteers developing antibody after the first polyvalent vaccine dose were 73 for population A and 46 for population B. After the following vaccine dose these proportions rose to 84% and 70% for populations A and B respectively. The better response observed with population A is considered to be due to a booster effect among volunteers previously vaccinated.

H. G. Pereira

GSELL, O. & MÄDER, H. Schutzimpfungen gegen Adenovirusinfektionen. Beobachtungen in schweizerischen Rekrutenschulen 1958. [**Vaccination against Adenovirus Infections. Observations in Swiss Recruit Units in 1958**] *Schweiz. med. Woch.* 1959, Mar. 21, v. 89, No. 12, 315–20, 1 fig. [Numerous refs.]

In February and March 1958 vaccination with an adenovirus vaccine containing types 1, 3, 4, 5 and 7 was carried out in 3 army establishments for recruits in Switzerland. A single dose of 1 cc. was given from a separate syringe at the same time as the first injection of tetanus toxoid; 589 men were vaccinated in all, and a similar number were left unvaccinated. Local or general reactions were not observed. The efficacy of the vaccine could not be assessed epidemiologically, since no cases of adenovirus infection occurred in the establishments

over a 3–4-month period of observation. Serological investigation carried out on 23 men showed that complement-fixing antibody appeared after 15 days but was no longer present after 3½ months. *D. J. Bauer*

JAWETZ, E. **The Story of Shipyard Eye.** *Brit. Med. J.* 1959, Apr. 4, 873–6, 2 figs. [18 refs.]

An historical account is given of shipyard eye, a condition which has been described under various names and is now usually known as epidemic kerato-conjunctivitis. The causative agent has been identified as adenovirus type 8, and up to the present time 100 strains have been isolated, mostly from patients suffering from the typical disease. It has not been possible, however, to carry out retrospective serological investigations of material obtained during the epidemics which occurred in the early 1940s. In tissue culture the yield of infective virus is very low, and represents only a small fraction of the total amount of specific antigenic material present. In serial examinations of material from the eyes of a technician who contracted a laboratory infection, only very small amounts of virus could be detected: this together with the absence of contact infections suggested that the amount of virus produced was insufficient to give rise to direct transmission, and that the direct introduction of a large amount of virus is required to cause infection. In Oriental countries type 8 adenovirus infection is mainly a disease of children, causing a systemic illness with only minor involvement of the eye, but in the United States, Great Britain and Canada it is suggested that the disease is mainly iatrogenic and is transmitted by infected instruments or solutions in ophthalmological clinics. *D. J. Bauer*

SMIT, P. **Acute Respiratory Disease in the African.** *Proc. Mine Med. Officers' Ass.* Johannesburg. 1959, Jan.–Feb., v. 38, No. 367, 92–101, 3 figs. [11 refs.] Discussion 101–3.

The gold mines situated on the Rand have had a well organized medical service since the beginning of the century, yet acute respiratory disease continues to provide a grave problem among the large African labour force which they employ. The favourable climatic conditions and good housing are neutralized by the high temperatures, humidity and cramped, crowded conditions which are inevitable at the working face. Pneumoconiosis has been greatly reduced in incidence and speed of development by scientific dust-control measures in recent years while prompt hospital care and the free use of chemotherapy and antibiotics have brought down the case mortality from respiratory disease to a very low level. Nevertheless the attack rate for acute respiratory infections remains very high and even shows a tendency to increase.

The fight against this menace makes interesting history. Between 1911 and 1913 Sir Almroth WRIGHT studied the bacteriology of pneumonia among the miners and introduced a prophylactic pneumococcal vaccine which appears to have had a beneficial effect. However, the influenza pandemic of 1919 was followed by a changed bacterial flora, to combat which a revised vaccine was introduced during the next few years. A similar change in the population of respiratory pathogens appears to have followed the Asian influenza A pandemic of 1957 with the result that, though the well-tried vaccine of earlier years is still given to that section of the labour force which is considered most susceptible [see below], its benefit is now very doubtful.

The African labour force comprises 3 elements; "Tropicals", coming from the countries lying north of 22° South latitude, "East Coasters" from Portuguese territory south of the Sabi River, and "British South Africans" who are natives of the Union of South Africa and Protectorates below 22° South latitude. Acute respiratory disease has always been more common among the "Tropicals" than in the other 2 groups, and the consequent mortality in this community was so high that their employment was discontinued between 1913 and 1934. While the "East Coasters" are less susceptible to respiratory disease than the "Tropicals", the lowest incidence of these diseases is shown by the "British South Africans". In any group a miner will show less susceptibility to acute respiratory disease during his second year than in his first, and less again if he is subsequently re-employed.

Since 1957 a detailed virological investigation has been carried out by the South African Institute of Medical Research virus laboratory under the direction of Dr. J. GEAR, the population studied being the African labour force employed in the Simmer and Jack mine, which has always shown the highest incidence of acute respiratory disease among all the mines in the vicinity. Although the Asian influenza A virus was isolated in 1957 and continues sporadically to attack new arrivals especially "Tropicals", in at least two-thirds of the patients clinically diagnosed as having "influenza" no specific viral agent could be recovered or serological evidence found. This is in keeping with world-wide experience [and illustrates the present immaturity of virological knowledge]. One fact of interest is that the adenoviruses do not appear to be at all prevalent in this community. *J. H. Walters*

MORRIS, J. C. H. **Staphylococcal Pneumonia treated with "Spontin".** *Med. J. Australia.* 1959, Aug. 1, v. 2, No. 5, 151–3.

"1. The clinical course of a desperately severe case of staphylococcal pneumonia is described.

"2. A dramatic response to ristocetin ('Spontin') was obtained. This drug is as yet available only in limited quantities, but in this case has shown itself to be a valuable weapon to be kept in reserve for staphylococcal infections not responding to other antibiotics. Its present very high cost makes its use unlikely in less severe cases."

LANE, W. F., WATLING, J. & MARSHALL, J. **A Case of Meningitis caused by** *Listeria monocytogenes. Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, July, v. 18, 127–30.

The eighth case to be recorded in Great Britain of meningitis due to *Listeria* [*Erysipelothrix*] *monocytogenes* is described. The patient was a man of 56 years

who made a rapid and uneventful recovery after treatment with penicillin, streptomycin, and chloramphenicol. The source of infection was not discovered. An account is given of the morphological, cultural, and biochemical characteristics of the organism isolated from the cerebrospinal fluid: it was agglutinated to a titre of 1 in 640 by 2 antisera prepared against the standard NCTC strain and a newly isolated strain of *L. monocytogenes*. No antibodies to the H and O antigens of the organism were detected in a specimen of serum taken from the patient 8 weeks after the onset of illness. The authors attribute this to the short duration of the illness.

Morag C. Timbury

KHOOBYARIAN, N., DRAPER, Janet, DWYER, A. C., MURTHY, Y. K. S. & WALCHER, D. N. **Some Viral Central Nervous System Diseases. Laboratory Studies with Emphasis on Aseptic Meningitis.** *J. Dis. Children.* Chicago. 1959, July, v. 98, No. 1, 15–23, 1 diagram. [23 refs.]

During the years 1956 and 1957, 245 patients with a diagnosis of poliomyelitis, meningitis, encephalitis or miscellaneous diseases of the central nervous system admitted to the James Whitcomb Riley Hospital for Children, Indianapolis, were examined extensively for the presence of viruses by modern methods. It was noted that the diagnosis on admission was changed during the course of the disease in over 10% of the patients. About 50% of the patients yielded a virus. 100 patients were diagnosed as suffering from poliomyelitis, 86 being paralytic and 14 non-paralytic. A distinction was drawn between non-paralytic poliomyelitis and abacterial meningitis on clinical grounds in that the non-paralytic poliomyelitis patients suffered from muscle spasm which was slight or absent from the abacterial meningitis patients. True muscle paralysis was not noted in any patient diagnosed as suffering from abacterial meningitis. 89 of the patients diagnosed on clinical grounds as poliomyelitis yielded poliovirus. An especially careful study was made on 52 patients who were suffering from meningitis and 21 of these yielded a virus. The viruses isolated were 1 Coxsackie A9, 3 B2, 4 B4, 8 B5, 1 ECHO 7 and 4 ECHO 9. There was good evidence that the Coxsackie strains were associated with infection in the majority of patients from whom they were isolated but there was no evidence of a rise in antibodies during the course of the disease in 2 persons excreting ECHO viruses so that their role was undecided. 13 out of 23 patients who did not yield a virus showed a high titre in both specimens to one or other of the viruses that were isolated in this study and 2 showed a diagnostic rise in antibody titre, but it is concluded that there is still much to learn about the aetiology of viral meningitis.

A. J. Beale

VAN LOGHEM, J. J. Pre-epidemische en epidemische wereldcijfers van poliomyelitis. [**Pre-epidemic and Epidemic World Figures for Poliomyelitis**] *Nederl. Tijdschr. v. Geneesk.* 1959, Apr. 18, v. 103, No. 16, 851–7, 3 charts.

A study has been made of the monthly incidence of poliomyelitis between 1953 and 1957 in 16 countries in the northern and 5 in the southern hemisphere. The minimum incidence was in March or April in the northern hemisphere; the epidemic rise began more or less simultaneously, but the peak incidence was reached at different times in different countries, ranging from August to October in the more northern countries and from June to July in Spain, Greece, Italy and Israel. In the countries of the southern hemisphere (Argentina, Brazil, Chile, South Africa and Australia) the minimum incidence was in September–October and the maximum in February–May.

D. J. Bauer

STEIGMAN, A. J. & LIPTON, M. M. **Poliovirus-Neutralising Antibody in Faeces of Poliomyelitic Children.** *Lancet.* 1959, Sept. 5, 272–3.

Preliminary information is recorded showing that poliovirus neutralizing antibody can be detected in faecal suspensions of cases of poliomyelitis. The types of antibody detected in faecal extracts are not always the same type as that causing the disease. Thus a patient with paralytic poliomyelitis excreting type 1 poliovirus is described who developed a titre of 1 in 80 to type 2 virus in the faecal extract on the 21st day. The serum titre against type 2 virus was 1 in 2,048. Evidence is presented that the poliovirus inhibitor in faecal extracts is antibody. These results are presented in the hope that other investigators will take the opportunity of testing faecal extracts for antibodies to all 3 types of poliovirus during the present epidemic of poliomyelitis in the U.S.A.

A. J. Beale

ANDRIEU, G., ENJALBERT, L., LAPCHINE, L., LARENG, M. B. & DIDIER, J. La poliomyélite dans le Sud-Ouest de la France. Étude épidémiologique et virologique. [**Epidemiological and Virological Study of Poliomyelitis in South West France**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Mar., v. 7, No. 2, 123–30.

This is a long account of the epidemiology of poliomyelitis in South West France in 1956 and 1957. The value of tissue culture methods in adding precision to epidemiological investigations is reaffirmed. In 1956 type 1 virus predominated and in 1957 type 3. Type 2 virus was not isolated from a case of poliomyelitis. The authors also reaffirm the importance of subclinical infections in the spread of poliovirus and the comparative frequency with which the "non-paralytic' poliomyelitis syndrome is due to agents other than poliovirus.

A. J. Beale

FLATO, S., GRODZICKA-KRÓLAK, Hanna & MALCZEWSKI, B., with the technical assistance of Helena SZYMANSKA. Izolacja i typowanie szczepow wirusa polio z przypadków epidemii w 1956 r. [**Isolation and Typing of Poliomyelitis Virus Strains from Patients during the 1956 Epidemic**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 1, 31–8, 2 charts. [18 refs.] English summary.

In isolation experiments in monkey kidney tissue cultures 126 strains of poliomyelitis virus and 8 unidentified strains were isolated from 255 stool samples

from patients suffering from poliomyelitis and other persons during an epidemic in Poland in 1956. 85 strains (67·5%) were type I, 31 (24·6%) were type II and 10 (7·9%) type III; 101 strains (80·1%) were obtained from 137 persons suffering from paralytic and 11 (8·8%) from 48 suffering from non-paralytic poliomyelitis, and 14 strains (11·1%) were obtained from 70 persons who on clinical grounds were considered not to be suffering from poliomyelitis, including 10 persons who had been in contact with the disease.

D. J. Bauer

MOSCOVICI, C., GINEVRI, A. & KEMPE, C. H. **The Distribution of Poliomyelitis and ECHO Viruses in a Children's Institution.** *J. Dis. Children.* Chicago. 1959, Aug., v. 98, No. 2, 139–43. [20 refs.]

A study of the viral flora of rectal swabs from normal children under 2 years of age was carried out in Rome in 1956 with monkey kidney cells. The children were in an orphanage with a continually changing population, and 416 healthy children were examined from January to August 1956. In addition a group of 52 newborn infants were surveyed for 1 year. This study once again illustrates the great frequency with which enteroviruses can be isolated from rectal swabs of normal children. The isolation rate for polioviruses was 13% and for other viruses 17·5%. All the polioviruses isolated from the children were type 2. Types 9, 11, 12, 13, 14 and 15 were represented in the 67 ECHO virus isolations, but ECHO 15 accounted for over one-half of the total isolations. In addition 6 strains of adenovirus were isolated, types 1, 2, 3 and 6 being represented. 51 viruses were isolated from a population of newborn infants studied during the year. Again the ECHO viruses predominated with type 15 being most prevalent (32%). In addition to type 2 poliomyelitis virus, type 3 was also isolated from the babies. The same types of adenovirus were found in the newborn infants as in the older children but in addition to the polio, ECHO and adenoviruses, 3 as yet unidentified agents were also obtained. Sera were tested from a few of the children and in general it was found that antibodies were present to the virus types that had been isolated from the children but not to other virus types, for example, 100% of the children examined had antibodies to type 2 poliovirus whereas only 11% had them to the type 1 virus.

[For earlier studies by the authors see this *Bulletin*, 1958, v. 33, 212 *bis*.] *A. J. Beale*

SCHMIDT, Nathalie J. & LENNETTE, E. H., with the technical assistance of Shirly HAGENS & Juanita DENNIS. **A Microflocculation Test for Poliomyelitis with Observations on the Flocculating Antibody Response in Human Poliomyelitis.** *Amer. J. Hyg.* 1959, July, v. 70, No. 1, 51–65. [18 refs.]

A modification of the microflocculation test with poliovirus and antiserum devised by SMITH *et al.* [this *Bulletin*, 1956, v. 31, 1172] is described in detail. The value of the method in the diagnosis of poliomyelitis has been compared with the complement-fixation (CF) and neutralization tests on paired sera from 53 patients (only 51 for the neutralization test) from whom a poliovirus was isolated (type 1, 41; type 2, 2; type 3, 10). 4-fold or greater rises in antibody titre were detected in 68% of the patients by the CF test, in 51% by the microflocculation test and in 37% by the neutralization test. The best combination of 2 tests was the CF and microflocculation tests which confirmed the virus isolation result in 86% of the patients. Every patient showed the presence of homotypic poliovirus flocculating antibodies in one or other serum sample. The microflocculation test proved very specific; a few patients had stationary titres to other virus types and these were usually mirrored by titres in the other 2 tests.

Paired sera from 22 patients who failed to yield poliovirus were also examined. 5 of these patients were excreting Coxsackie B5 but none of them showed a rise in poliovirus flocculating antibodies. Low levels of antibodies were present in a greater proportion of the poliovaccinated than the unvaccinated individuals. Similar results were obtained with the CF test. The defect of the microflocculation test was the early appearance of antibodies. The results on a few patients suggest that the antibody levels also decline early in convalescence, and the authors believe that the possibility that a titre in the acute phase serum may be diagnostic is worth investigating. At present the microflocculation test is not recommended as a diagnostic procedure, both because it is not as sensitive as the CF test and also because the antigens are rather difficult and expensive to prepare. *A. J. Beale*

AINLEY, N. J. **Gastro-Intestinal Lesions in Bulbar Poliomyelitis.** *Irish J. Med. Sci.* 1959, Aug., 6th Ser., No. 404, 368–70. [14 refs.]

"Two fatal cases of bulbar poliomyelitis are described.

"There was acute ulceration of the oesophagus, stomach and duodenum accompanied by haematemesis in the first patient. Involvement of the hypothalamus and the central autonomic pathways is thought to be the cause of the gastro-intestinal ulceration.

"The second patient died from rupture of the oesophagus. This was due to persistent vomiting, and possibly inco-ordination of the pharyngeal muscles as a result of the brain stem lesions."

GELFAND, H. M., POTASH, L., LEBLANC, Dorothy R. & FOX, J. P. **Intrafamilial and Interfamilial Spread of Living Vaccine Strains of Polioviruses.** *J. Amer. Med. Ass.* 1959, Aug. 22, v. 170, No. 17, 2039–48, 1 fig. [14 refs.]

Since 1953 Dr. Fox and his colleagues have been carrying out a careful study of the natural history of polio and other enterovirus infections in a group of families in New Orleans [this *Bulletin*, 1958, v. 33, 931]. They had previously found that the administration of Salk vaccine in 3 doses had failed to influence the spread of polioviruses in their survey population. In 1958 a group of 56 family units each containing at least 3 naturally susceptible individuals were recruited for a

study of the effect of Sabin's strains of attenuated poliovirus. A naturally susceptible individual is one who has no antibodies for a particular type of poliovirus as measured by lack of inhibition of the cytopathic effect of that virus on monkey kidney tissue cultures before the administration of killed vaccine. All the persons over 6 months old admitted to the trial had been vaccinated with killed poliovaccine. The course consisted of 2 primary doses followed by a booster dose. 1 of the 3 naturally susceptible members of a family unit was infected by the oral route with the appropriate type of attenuated poliovirus. The virus dose was estimated to be about 100,000 to 10 million infectious particles but a few people by mistake received only about 4,000. The results of these feedings were followed by taking samples from the individuals fed, from their family contacts and from the contacts outside the family. The results were as follows:—

(1) *Infection of persons given virus*

There were 51 feedings and 46 resulted in the excretion of the appropriate type of poliovirus in the faeces. 4 of the failures were given only 4,000 infectious doses of virus. Pharyngeal excretion was rare in the people given 100,000 infectious doses but occurred in 16 out of 22 given 10 million or more infectious doses. The duration of excretion was very variable, up to a maximum of 17 days from the pharynx and well over 100 days from the faeces.

(2) *Spread of infection in the family*

The virus spread to susceptible family contacts with considerable frequency but this was not as great as the spread of wild polioviruses under similar circumstances. The spread was more pronounced for type 3 than for other types of attenuated poliovirus and was more prevalent in the lower than in the higher socio-economic family units. It was also slightly more prevalent in persons given the larger dose of virus who were also more likely to excrete virus in the pharynx. Spread of infection from adults was not observed despite the fact that some of these excreted poliovirus in the pharynx, but all these adults were in the higher socio-economic group. Quite a large number of successful contact infections occurred in people who were naturally immune.

(3) *Spread outside the family*

Extra-familial spread did occur but appeared somewhat variable. 4 units were studied and in 2 no spread occurred. Many of the contacts tended to excrete virus for shorter periods, particularly those who were naturally immune. In one of the units giving a single 2-hour period of contact an index child infected with type 3 transmitted infection to 2 out of 3 child visitors, and in another unit a similar 2-hour contact period between 3 child visitors and 4 infected children resulted in the transmission of infection to only 1 of the susceptible children.

(4) *Interference*

This was suggested on several occasions. Although the administration of the virus to the index child resulted in a successful infection, the subsequent spread to contacts, especially in the lower socio-economic family units, was sometimes prevented by intercurrent household infection with other viruses. This occurred not only with wild poliovirus infection but also with other members of the enterovirus family.

(5) *Isolation of virus in infected households*

Attempts were made sporadically to isolate poliovirus from the skin or from toys, doorknobs or floors. In 5 units poliovirus was isolated. This was either from the skin of the buttocks or from the fingers in 4 units. In one family, however, a wild type 2 poliovirus was found in a swab from the living room floor after the children had been fed on Sabin's type 1 poliovirus.

(6) *Antibody response*

As yet not all the subjects have been tested for an antibody rise but the results appear to show that people without antibodies to the type of attenuated poliovirus infection acquired will develop a good antibody response. Thus, only 2 out of 23 with a titre of less than 1 in 10 before infection failed to develop a titre of at least 1 in 80. One of these 2 still had a titre of less than 1 in 10 and the other a titre of 1 in 10 exactly. An antibody titre of over 1 in 40 either acquired as the result of administration of Salk vaccine or in naturally immune individuals is usually unaffected by infection with attenuated poliovaccine, the titre after a successful alimentary infection remaining the same as before that infection.

(7) There was no evidence that any illness in the children under study was due to the administration or the spread of the attenuated poliovirus strains.

A. J. Beale

GRIST, N. R., DUNCAN, I. B. R., LANDSMAN, J. B. & STEVENSON, J. **"Not Poliomyelitis".** *Lancet.* 1959, Sept. 19, 386.

The value of virological diagnostic methods in elucidating the aetiology of meningitis is illustrated. Experiences in the West of Scotland in 1958 and in 1959 are contrasted. In July and August 1958, 85 specimens from patients with paralytic poliomyelitis and 89 from patients with meningitis were received. Poliovirus was the only agent isolated from both groups of patients. In 1959 in the same months 10 specimens from paralysed patients and 96 from those with meningitis were received. No polioviruses were isolated but a small proportion of stools yielded other enteroviruses (Coxsackie A9, B2 and 5) in tissue culture. Thus far 4 out of 5 specimens negative in monkey kidney tissue culture have yielded agents (presumably Coxsackie A viruses) pathogenic for suckling mice. The clinical features of the cases of "aseptic meningitis" are described. These included muscle weakness in 8 out of 30 patients, in 6 sufficiently severe to require physiotherapy for residual limb weakness. The clinical features might have suggested an outbreak of mild poliomyelitis perhaps modified by vaccination. This conclusion is not supported by the studies in the

virus laboratory. [The complete results of the investigation will be awaited with interest.] *A. J. Beale*

WISSLER, H. & WIESMANN, E. Die Zürcher "Sommergrippe" 1958. Isolierung von Coxsackie-Virus B1. ["**Summer Influenza" in Zürich in 1958. Isolation of B1 Coxsackie Virus**] *Schweiz. med. Woch.* 1959, June 6, v. 89, No. 23, 608–10, 1 fig.

During the summer of 1958 an epidemic occurred in Zürich characterized by fever, pharyngitis, headache, meningism and in some cases vomiting and abdominal pains. Children were mainly affected. A morbilliform eruption which was usually fleeting and localized to the face and trunk was occasionally observed. 12 strains of group B Coxsackie virus were isolated from 14 stool samples, and 3 strains were identified as type B1. In 6 convalescent-phase sera type B1 neutralizing antibody was present in titres of 80–320. No strains of ECHO or poliomyelitis virus could be isolated.

D. J. Bauer

SODE, J. & BAKER, W. J. **Acute Benign Pericarditis and Pneumonitis associated with Coxsackie Virus Group B, Type 2 Infection in a Young Man.** *Arch. Intern. Med.* 1959, Aug., v. 104, No. 2, 313–17, 2 figs. [13 refs.]

"A case of acute benign pericarditis and bilateral pneumonitis, meeting suggested criteria for Coxsackie virus disease is presented. The history, the physical and laboratory findings, and the clinical course are discussed."

RANNON, L., GOLDBLUM, N., LEVENTON, Z., LEVI, M., FARIN, J. & PUSHKIN, W. [**An Outbreak of ECHO 9 Disease in Israel**] *Harefuah.* Jerusalem. 1959, Sept. 1, v. 57, No. 5 [In Hebrew 115–18. English summary 118].

The English summary appended to the paper is as follows:—

"An outbreak of aseptic meningitis syndrome occurred in the settlement 'Haogen' in the Shomron area during the autumn of 1958. Clinical and laboratory studies were carried out on the patients and on a number of contacts and controls. 22 cases with meningitis and 13 abortive cases were concentrated chiefly among children 4 to 10 years of age; few cases occurred in infants and adults. The clinical picture of the disease was fever of 2 to 10 days duration, in some cases biphasic, headaches, vomiting, somnolence and meningeal signs. In most cases there was a tendency towards hyperreflexia. Exanthems were absent in all the cases studied. Among the meningitis cases two developed flaccid paresis of the lower limbs, and one of them still had some leg weakness on follow up examination three months after onset.

"The laboratory investigations included attempts to isolate viruses from stools and throat swabs as well as tissue culture neutralization tests. 12 monkey kidney cell cytopathic agents were isolated from 8 patients and from one contact. All strains proved to be immunologically related or identical with ECHO virus type 9.

"Tissue culture neutralization tests for ECHO 9 antibody were carried out on blood samples taken during the acute and convalescent phase of the disease. In many cases, four-fold or higher rises in antibody titer were observed. 87 per cent of the meningitis cases and 85 per cent of the abortive cases proved positive for ECHO virus 9 infection. Most of the controls were devoid of ECHO 9 antibodies.

"Of special interest were the observations on the mouse pathogenicity of Israel ECHO 9 isolates. All 12 strains were pathogenic for infant mice following isolation in monkey kidney cell monolayers and showed histologically a similarity to Coxsackie A myositis. On isolation, the strains showed marked variation in virulence for infant mice. These findings are discussed in the light of present knowledge of ECHO 9 disease in Europe and the U. S. A."

BÁRDOS, V., ADAMCOVÁ, J., ŠIMKOVÁ, A., ROSICKÝ, B., MRCIAK, M. & DANIEL, M. Prírodne ohnisko klieštovej encefalitídy vo Vysokých Tatrách. [**A Natural Focus of Tick-Borne Encephalitis in the High Tatras**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 3, 145–52, 1 fig. [17 refs.] English summary.

In an investigation of a natural focus of tick-borne encephalitis in the High Tatras, Slovakia, attempts were made to detect the virus in the brains of small rodents and insectivores caught in the area. By the intracerebral inoculation of mice 4 strains of virus were isolated from 4 of 34 pooled brain suspensions obtained from 62 animals. The strains were identified as tick-borne encephalitis virus by neutralization tests with reference antiserum. The species from which they were obtained were *Sorex alpinus, Mus musculus, Apodemus flavicollis* and *Arvicola terrestris.* Neutralizing antibody was found in the sera of these species and also in *Pitymys subterraneus, Microtus agrestis* and *Clethrionomys glareolus,* but not in the sera of 24 domestic animals and 61 persons living in the area.

D. J. Bauer

BEADLE, L. D. **Field Observations on the Biting Habits of *Culex tarsalis* at Mitchell, Nebraska, and Logan, Utah.** *Amer. J. Trop. Med. & Hyg.* 1959, Mar., v. 8, No. 2, Pt. 1, 134–40, 3 figs. [17 refs.]

Culex tarsalis is the main vector of western and St. Louis encephalitis in the western half of North America. Human bait catches in Nebraska and Utah showed that 20–52% of the total biting population belonged to this species, both in the town and in the country. Consecutive 15-minute collections, beginning at sunset and continuing for 2 hours, showed a peak of biting activity beginning 30 minutes after sunset (end of twilight), and continuing for 1 hour. Photometer readings at sunset showed mean readings of 5·3 and 7·5 foot candles in two localities and, when the light intensity was diminished to 0·2 foot candles, this reading usually corresponded with the first wave of biting activity. The decline in activity after the peak is believed to be governed by falling temperature; on

warm nights the period of maximum biting activity was prolonged.

Light trap and bait catches gave similar seasonal distributions of the abundance of this species, although light trap catches in towns were lower, possibly owing to competition with other light sources. Precipitin tests on 446 engorged females showed that 431 had fed on passerine birds, 3 on cattle and 12 showed no reaction. Bait catches also showed that this species is attracted by chickens, sheep and horse. It appears that *Culex tarsalis* feeds readily on a wide range of hosts and that the availability of the host determines the type of blood meal taken. *B. R. Laurence*

COPPS, S. C. & GIDDINGS, L. E. **Transplacental Transmission of Western Equine Encephalitis. Report of a Case.** *Pediatrics.* Springfield, Ill. 1959, July, v. 24, No. 1, 31–3.

A 6-day-old infant developed fever and convulsions, the mother having had a febrile illness for 10 days before parturition. The baby had signs of encephalitis and the cerebrospinal fluid contained 477 cells per cmm. (96% lymphocytes), 60 mgm./100 ml. sugar and 240 mgm./100 ml. protein. Soon after admission to hospital the infant started to have periods of apnoea which increased in frequency and duration. On the following day steroid therapy commenced. Within 24 hours oedema appeared in the face and limbs. The steroid dosage was reduced and the child's condition improved but apnoea persisted, although it was less frequent, and there was a fine, intermittent tremor. By the 6th day the infant's condition was good and he was discharged from hospital on the 16th day. On discharge he had nystamus and "disorganized" limb movements. 6 months later the child was retarded in development and there was spasticity of the limbs.

A 16-fold increase in haemagglutinin-inhibiting antibody to western equine encephalomyelitis virus was demonstrated in the infant's serum, when specimens 3 days and 8 weeks after onset were compared. 19 days after onset of her febrile illness the mother's serum had an antibody titre of 320 falling to 80, 8 weeks later. This evidence strongly suggests that the infant was infected by the transplacental route.

[For a previous case, see this *Bulletin*, 1954, v. 29, 139.] *C. E. Gordon Smith*

GIDDINGS, L. E., COPPS, S. G. & SOOTER, C. A. **Infectious Encephalitis in Colorado.** *Pub. Health Rep.* Wash. 1959, July, v. 74, No. 7, 647–52, 3 figs.

258 cases of encephalitis of probable infectious origin reported in Colorado between May 1956 and the end of 1957 have been studied epidemiologically. Sera from 125 patients were tested for antibody responses to a variety of agents and by the laboratory and clinical means the diagnosis or probable diagnosis of St. Louis encephalitis was made in 38% and of western equine encephalomyelitis in 20%. 22% of the patients were diagnosed as mumps encephalitis mostly on clinical grounds. Other causes recognized in order of importance were poliomyelitis, measles, Colorado tick fever, and post-vaccinal encephalitis. ECHO antibodies were found in some patients, but their significance could not be determined. The aetiology of 149 of the 258 cases (58%) remained unknown. There were 10 deaths.

The age incidence of western equine and mumps infections and of the cases of unknown aetiology were predominantly in persons under 20 years of age. St. Louis infections were evenly spread through all age-groups. The seasonal distribution of western equine and St. Louis infections was from July to October with the peak in August, while mumps cases occurred throughout the year with a low peak in April–June. [The titles of Figures 2 and 3 have been transposed.] *C. E. Gordon Smith*

SANMARTIN, C. & DUEÑAS, A. **Hemagglutination-Inhibition and Neutralization Tests for the Venezuelan Equine Encephalomyelitis Virus.** *Amer. J. Trop. Med. & Hyg.* 1959, May, v. 8, No. 3, 346–8. [12 refs.]

487 human sera were collected in various parts of Colombia. They were tested by a neutralization test and haemagglutinin-inhibition test with the Kubes-Rios strain of Venezuelan equine encephalomyelitis virus. The neutralization tests were with undiluted serum tested against a single dose of 50 to 150 LD50 of virus. Bentonite or kaolin extraction was used for the sera in haemagglutinin-inhibition tests.

344 sera had no haemagglutinin-inhibiting antibodies and were also negative in the neutralization test. 100 sera with titres of 1 in 80 or higher, all had positive neutralization tests. Of the 43 sera with titres less than 1 in 80, 30 had positive neutralization tests. Of the remaining 13 sera, 10 were tested against other group A arboviruses and high levels of antibody were demonstrated in 9 of them against Mayaro virus.

The authors concluded that a haemagglutinin-inhibition titre of 1 in 80 or higher could be taken as certainly indicating a presence of neutralizing antibodies. [This conclusion should be accepted with caution in view of the frequent occurrence of cross-reactions where multiple infections are likely to have occurred.] *C. E. Gordon Smith*

SCHAEFFER, M., GAJDUSEK, D. C., LEMA, A. B. & EICHENWALD, H. **Epidemic Jungle Fevers among Okinawan Colonists in the Bolivian Rain Forest. I. Epidemiology.** *Amer. J. Trop. Med. & Hyg.* 1959, May, v. 8, No. 3, 372–96, 14 figs. [13 refs.]

403 immigrant Okinawans, comprising complete families, were settled in an area (Uruma) of unexplored rain forest east of the Rio Grande in August–September 1954. In October–November there were 3 cases of severe febrile illness, one of them fatal and similar cases continued to occur until the settlement was abandoned in July 1955. The nearest settlement of indigenous people was 12 km. away. The Okinawans were housed in 3 large buildings divided into family cubicles. In all, 192 of the 403 inhabitants suffered a febrile illness. Both sexes and all ages were similarly affected except that children under 5 were less often

affected. Illnesses were not more frequent in families where a case occurred than in the whole community. Of 15 deaths, 3 were in children. Clinically there were no specifically diagnostic features except that most cases had (a) a sudden onset of fever lasting 3–7 days; (b) moderately severe headache lasting 2–3 days; (c) profuse sweating; (d) polyuria preceding the onset of fever and lasting 1–2 days after; and (e) tachycardia out of proportion to the temperature. Convalescence averaged 10 days. Death occurred between the 3rd and 8th days after onset.

Uruma virus (related to Semliki Forest virus and in the Casals group A) was isolated from the blood of 2 patients and high titres of neutralizing antibody to this virus were found in convalescent sera from 3 of 38 patients. Probably only 10–15% of cases were due to Uruma virus. Varying numbers of sera from a collection of 100 were tested against a wide variety of diagnostic reagents and no significant positive findings resulted. 66 sera were collected from the nearest indigenous settlement and 38% had antibody to Uruma virus. *C. E. Gordon Smith*

WORK, T. H., RODERIGUEZ, F. R. & BHATT, P. N. **Virological Epidemiology of the 1958 Epidemic of Kyasanur Forest Disease.** *Amer. J. Pub. Health.* 1959, July, v. 49, No. 7, 869–74, 3 figs.

This is a review of the epidemiology of Kyasanur forest disease [this *Bulletin*, 1959, v. 34, 203 *ter.*] up to the middle of 1958. The first cases of the disease probably occurred in January 1956. The virus was first isolated from the blood of a moribund monkey (*Presbytis entellus*). In each year, 1956–8, the disease has appeared in early spring and continued until midsummer, but virus isolation from man, monkeys or ticks have been made in every month of the year except November and December. Each year the area affected by the disease has increased: from only 4 villages in 1956 to more than 20 in 1957. An early monsoon in 1958 brought the epidemic to an end 6 weeks sooner than 1957 and there were therefore fewer cases and less extension of the distribution in 1958. The clinical picture is described and diagnosis by isolation of the virus from blood has been very successful. The vector appears to be *Haemaphysalis spinigera* and antibody studies suggest that many monkeys survive the disease. *C. E. Gordon Smith*

SEAL, S. C. **An Outbreak of Encephalitis in Nagpur in 1958. A report of Brief Investigation.** *Indian J. Pub. Health.* 1959, Apr., v. 3, No. 2, 147–59, 1 map and 1 diagram.

An epidemic of encephalitis was recognized in Nagpur, India, in the summer of 1958. The disease was first diagnosed in a child admitted to hospital in mid-June, and thereafter 140 more patients were treated in the two large hospitals serving the city, between that date and the middle of August. The highest rate of hospital admission for this disease was during the first week of July, but a high level was maintained until the end of that month. The patients were predominantly infants and young children; only 3 admitted to hospital were older than 15 years. The disease was more virulent in the initial than in the later weeks of the epidemic. The numbers of admissions and the deaths by age-groups were as follows:—

under 2 years		35	admissions	13	deaths
2–5	„	36	„	14	„
6–10	„	51	„	24	„
11–15	„	12	„	3	„

The overall case mortality among the hospital patients in whom this diagnosis was made was 41·4%.

The disease was of abrupt onset with fever, rigors or convulsions together with alimentary symptoms, which usually comprised vomiting and diarrhoea. Neurological symptoms were typically generalized and never focal; they included drowsiness, tremors, and spinal rigidity. In fatal cases death usually occurred in coma within 24 hours of admission, from loss of peripheral vascular tone. Some patients showed one and occasionally two relapses, which were milder and shorter than the initial illness. Acute inflammation of the throat with ulceration was noted in some children. In severely affected patients the knee jerks were lost and in a few an extensor planter response was obtained, while signs of meningeal irritation were obvious. The incubation period might be as short as 4 days. [The clinical details given are scanty, for no mention is made of the duration of the illness or the presence or absence of a rash.] There was no characteristic deviation of the leucocyte count. The cerebrospinal fluid was examined in 30 patients, in whom it was found to be under increased pressure with an excess of protein and a reduced sugar content, but with no pleocytosis. No recognized bacterial pathogens could be grown from blood, cerebrospinal fluid, stools, urine or throat swabs, and no viruses could be isolated in young white mice, or in tissue culture. [The sources of material inoculated are not stated.]

The author personally carried out a field survey of this disease which elicited several interesting facts. It was at once obvious that the disease was not confined to children, but was widespread among adults as a short-term fever of 24 hours' duration, characterized by headache, neck and back pains and sore throat. Multiple cases had sometimes occurred in one household. Moreover, it appeared that the disease was by no means new, many practitioners recalling similar cases in previous years. It was only the epidemic proportion of the 1958 outbreak that was novel.

The survey revealed a deplorable standard of public health. Only about a quarter of the houses had any sort of latrine: "The people could do without a latrine as the city wards except for the congested parts, are fairly widely dispersed with open lands in between that can be used for defaecation in a primitive way. All drains in the city are open and stink badly in many places." Exceptional drought had led to the formation of innumerable isolated pools in the beds of the water-courses in which mosquitoes, mostly culicine, were breeding abundantly. Fly breeding was also very profuse. The public water supply was from 3 different sources, of which only one was subjected to efficient filtration and chlorination. Open wells were widely used.

The author concludes that the epidemic was due to a virus transmitted by either flies or culicine mosquitoes, whose breeding had been facilitated by exceptional climatic conditions; the possibility of a water-borne infection was considered to be remote owing to the multiplicity of the sources used.

[This paper should be read by all those who hesitate to obtain what protection they can by TAB and polio-vaccine before travelling to India.] *J. H. Walters*

MANCHANDA, S. S. & GUPTA, H. L. **Acute Epidemic Encephalitis in Children at Amritsar (an Analysis of 45 Cases).** *Indian J. Child Health.* 1959, July, v. 8, No. 7, 341–8, 1 fig.

45 children admitted to hospital in Amritsar with the following criteria were studied: (1) fever of definite onset; (2) sensory disturbances, drowsiness or coma; (3) normal or almost normal cerebrospinal fluid; (4) no history suggestive of other causes. The children were aged 8 months to 11 years, 78% being between 2 and 8 years old. Most of the cases occurred in July–August 1958.

73% had a leucocyte count over 10,000 per cmm., 46% had gastro-intestinal disturbances. Unconsciousness, convulsions, rapid respiration and peripheral circulatory failure were common.

26 of the 45 died. Early in the outbreak the mortality was 74% falling to only 21% of the last 14 patients.

Nothing is known about the aetiology of these illnesses. *C. E. Gordon Smith*

ORMAY, L., ARADI, M. P., NIKODÉMUSZ, I. & LOSONCZY, G. Haemorrhagiás nephroso-nephritis góckutatása Magyarországon. [**An Investigation of a Focus of Haemorrhagic Nephroso-nephritis in Hungary**] *Népegészségügy.* Budapest. 1959, Jan., v. 40, No. 1, 18–24. [46 refs.] German summary.

In 1954–5 a parasitological investigation was carried out in a focus of haemorrhagic nephroso-nephritis in the neighbourhood of Tapolca, Hungary, where a number of persons working in the forests had been affected by the disease. Among 596 small mammals caught in the area *Apodemus flavicollis* (348 specimens, 58%) and *Clethrionomys glareolus* (206, 35%) predominated; these species rapidly increased in numbers in June and reached a maximum in the autumn. Among 7,705 parasites collected from the animals there were 3,831 trombiculid mites (49%), 1,768 *Laelaps* sp. (23%) and 940 *Ixodes* sp. (12%). Mice inoculated intracerebrally with a suspension of trombiculid mites showed signs of nervous involvement, but the condition could not be transmitted through more than 2 passages. Complement-fixation tests carried out with human convalescent sera and antigens consisting of aqueous extracts of the kidneys of rodents caught in the area indicated that 1% of the animals were infected with the agent. *D. J. Bauer*

ACKERMAN, H. R., RABKIN, R. & CAVVADAS, A. **Typhoid Fever: Clinical Features.** *South African Med. J.* 1959, Aug. 1, v. 33, No. 31, 637–9.

Any high fever, sustained for more than a week, in South Africa is likely to be due to typhoid. The authors, who draw on their experience at the City Hospital for Infectious Diseases, Cape Town, make certain points which are of importance.

Intestinal perforation is now always treated conservatively, the patient being nursed in Fowler's position, continuous gastric suction being instituted while all feeding and medication are given by parenteral routes. A pelvic abscess may result and may require subsequent surgical drainage. Chloramphenicol therapy should be maintained for 14 days in the uncomplicated case. Though steroid therapy may be required in the control of grave toxicity, its general use is to be condemned as dangerous. Convalescence should be carefully managed and the patient should not be allowed out of bed until the middle of the 5th week. For proof of cure, at the end of the 3rd week a Vi agglutination test is carried out and 3 [successive] specimens of faeces and urine are cultured. If all are negative the patient can be released from isolation.

If the Vi test or cultures prove positive, a carrier state is suspected and 10 successive cultures of the excreta at 5-day intervals are required. Only if all are negative is the patient released. In the treatment of the established carrier, a further trial of chloramphenicol should be made, "say 3 courses with an interval between". If this proves ineffectual, a trial should be made with tetracycline before resort is made to surgical measures. [This advice will not receive general acceptance as chloramphenicol has almost universally been reported as useless in the faecal carrier state, though massive penicillin therapy will sometimes prove successful.] *J. H. Walters*

LIPKIN, M. E. **Effect of Intervals and Number of Inoculations on the Immunological Response to Typhoid-Paratyphoid and Dysentery Vaccines. II. The Change of Immunological Reactivity during Different Systems of Vaccination and Revaccination.** *J. Microbiol., Epidemiol. & Immunobiol.* London 1957, v. 28, Nos. 7/8, 968–74, 3 figs. [Translated from Russian.]

The author has already shown by active protection tests in animals that two doses of vaccine with a 20-day interval is superior in protective value to 3 doses with 7–10-day intervals. In this paper he records the results of trials in human subjects, not previously immunized, with a tetravalent vaccine. Two batches of 50 young adults in each group were used for the test and the same typhoid-paratyphoid-dysentery (Flexner + Sonne) used for both groups. The first received 0·5, 1·0 and 1·0 ml. at 10-day intervals and the second batch of 50 were given 0·5 and 1·0 ml. with an interval of 20 days between the 2 doses. The volunteers were bled before inoculation and at 1, 3 and 6 months after the last dose of the vaccine. The mean agglutinin titres against living suspensions of typhoid, paratyphoid B, Flexner and Sonne dysentery bacilli were consistently

higher in all the specimens of sera from individuals receiving 2 doses of vaccine with the 20-day interval than in those receiving 3 doses at 10-day intervals. In mouse passive protection tests results of the same order were obtained although they were not so striking; the superiority was more obvious in the case of typhoid and Flexner bacilli than paratyphoid and Sonne bacilli.

6 months later the 2 groups were revaccinated. The 3-dose 10-day-interval group received 0·5 and 1·0 ml. of the tetravalent vaccine and the 2-dose 20-day-interval group received a single dose of 1·0 ml. of the same vaccine. In general it appeared that the single booster dose was adequate although there were not very significant differences between the two. The author recommends that service recruits should receive their primary vaccination of 2 doses with 20-day intervals in the autumn and that the single booster dose should be given in the following spring. No further inoculations against this group of diseases should be required for a period of 2 years. *H. J. Bensted*

Russu, V. V., Vlădoianu, I. R., Naș, Ligia, Muscan, S., Blasiu, H., Dăncilă, E. & Totesco, E. Contribution à l'étude de l'efficacité des méthodes entérales de vaccination T.A.B. [**Contribution to the Study of the Efficiency of Enteral TAB Vaccination**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Mar., v. 17, No. 1, 45–62, 11 graphs. [26 refs.]

These authors have re-investigated the possibilities of immunization against the enteric group of fevers by the oral administration of a TAB vaccine first introduced some 40 years ago (Besredka, *C.R. Acad. Sci.*, 1918, v. 167, 212 and a number of other papers in the following years). It will be recalled that although Besredka was able to show that his method resulted in the production of antibodies in rabbits it was the general opinion that his far reaching conclusions were not warranted by the experimental evidence.

In the present paper Dr. Russu and his colleagues compare the results of their serological investigations in human volunteers receiving only orally administered vaccine, a combination of oral and subcutaneous methods and the normal subcutaneous method. The oral vaccine consisted of TAB (1×10^9/ml.) 10 ml. mixed with 10–20% alcohol—3 doses at 2-day intervals. The combined method employed the same 3 doses of oral vaccine, but 25 days after the last dose, 0·5 ml. of the standard TAB vaccine was injected subcutaneously. All the subjects were bled before inoculation and 30 and 90 days after. The sera were tested for TH, TO, BH, BO, TVi agglutinins, TVi haemagglutinins and TVi complement fixing antibodies. The sera were also examined by the passive mouse protection test.

The results showed that although oral vaccination produced all the antibodies investigated the titres were generally low and mouse protection was poor. On the other hand the combined method gave agglutinin titres —O and Vi—which were not significantly different from those obtained with the standard subcutaneous TAB vaccine, and the protective antibodies, as measured by the mouse passive protection test, were in many cases slightly superior. The authors discuss the advantages and disadvantages of the three methods and feel that the results obtained with the combined oral and subcutaneous methods are sufficiently promising to warrant further work and field trials are now in progress. *H. J. Bensted*

Henze, B. Das endemische Vorkommen der bakteriellen Ruhr bei Flüchtlingen und einheimischer Bevölkerung. [**Endemic Incidence of Bacillary Dysentery in Refugees and the Indigenous Population**] *Öffentl. Gesundheitsdienst.* Stuttgart. 1959, July, v. 21, No. 4, 139–48, 3 figs.

This is a careful statistical and epidemiological account of the experience of bacillary dysentery during 1954–7 among the indigenous inhabitants of and the refugees to West Berlin which is based mainly on the records of about 5,000 cases of proved Sonne dysentery. The peak of incidence was in 1955 when 2,000 proved cases of infection occurred. Of these, 530 (216 clinical cases and 314 carrier cases) were in inhabitants of West Berlin and 1,470 (217 clinical cases and 1,253 carrier cases) among refugees. These figures are analysed by month, and by age and sex distribution and are also compared with the lesser incidence of the infection in various districts of the Federal Republic.

Nearly three-quarters of the cases of infection occurred among refugees of whom there were about 300,000 in the 4-year period. Accurate comparison of this incidence with that in the original inhabitants is not possible but it is estimated that the morbidity rate was 29·3 per 10,000 among the former as against 2·7 among the latter. Even more striking are the figures of comparison for the age-group 0–6 years which are estimated at 180 and 9·8 respectively. In the discussion it is noted that in refugee camps dysentery infection constantly occurred in those which accommodated more than 1,000 persons but that real epidemics were not observed. In the smaller camps of up to 100 persons, however, dysentery infection occurred in only one-sixth but then it was experienced as an epidemic affecting up to 50% of the camp population.

M. E. Delafield

Demina, A. A. **The Degree of Infection of Domestic Utensils with Dysentery Bacilli in Foci, and its Importance in Epidemiology.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1479–84. [11 refs.] [Translated from Russian.]

The investigation was carried out in a particular district of Moscow where dwellings were of the barrack type without main water and drainage; drinking fountains and primitive outside lavatories were used and there were many flies. 31·4% of the population were children up to the age of 15. The incidence of dysentery was highest in July and August, and 51–59% of the cases were in children; 70% of affected children were under 3 years of age. 20 areas (foci) of acute and 20 of chronic dysentery were observed, and 20 flats free from dysentery over the observation period of 2 years were used as controls. Washings

were taken from common domestic articles, *e.g.* furniture, linen, crockery and toys, and also hands and parts of buildings. Sterile cotton wool swabs moistened with 10% bile broth were rubbed over an area 10 by 20 cm., scrapings from the surface of a similar area of linen were likewise moistened with 10% bile broth. When necessary a 1% solution of thiosulphate was used to neutralize the effect of chlorine. The degree of contamination with dysentery bacilli varied from 2·9% (acute foci) to 5·3% (chronic foci), and was therefore highest in the chronic dysentery areas. Many of the strains isolated from the acute foci are described as "atypical". 5–8% positive results were obtained from furniture, 3–4% from crockery and 2–3% from linen. *Sh. flexneri* was isolated in a few instances. Fresh cases of dysentery were recorded only in foci where there were chronic dysentery patients at an acute stage of the disease.

It is suggested that the distribution of dysentery depends directly on the degree of bacterial contamination of utensils, and on a continuous state of contamination. Typical dysentery bacilli and atypical bacilli reverting to typical are important in epidemiology, but the part played by stable atypical bacilli in the transmission of infection is thought to be doubtful.

It is also suggested that examination of articles in everyday use in areas of infection may serve as a supplementary method of diagnosing dysentery.

Betty C. Hobbs

Levi-Jovovic, Eva, Zdravkovic, A. & Mikic-Jokovic, Mirjana. [**The Dominant Ways of the Transmission of Intestinal Infections in the Area of Prizren**] *Bull. Inst. Hyg.* Belgrade. 1959, v. 8, Nos. 1/2, 71–8. [16 refs.] [In Serbian.]

The English summary appended to the paper is as follows:—

"During our work in Prizren in 1958 we studied the various ways of transmission on pathogenic intestinal bacteria: drinking water and sewerage, food stuff, house flies and washouts from hands. Our investigations included not only households whose members carried various Shigellae but also the public buildings and epidemic focuses discovered during our investigation in Prizren and surroundings.

"1) *Drinking water.* Shigellae were not found in 23 samples of drinking water from two wells in households. In 156 samples from public drinking wells Sh. boydi 8 was found in only one case and that was from a public fountain.

"2) *Sewerage.* 89 samples were examined by direct inoculation of the definite quantities of water and 46 samples were taken with rolled strips of gauze (according to Moore's method). In directly inoculated samples the pathogenic enterobacteria were found 5 times (Sh. flexneri 2a twice, and Sh. flexneri 4, Sh. boydi 2 and S. typhi once). Using the rolled strips of gauze, in one sample was found S. typhi and in another one Sh. flexneri 6 var. Manchester and Sh. boydi 2 were found simultaneously.

"3) *Food stuff.* In 95 examined samples of food stuff neither Shigella nor Salmonella were found.

"4) *House flies.* 198 house flies from three households were examined and in one Sh. flexneri 1a was isolated 5 times and Sh. Schmitzi once. Out of 204 house flies collected in different public places, 4 were contaminated with Shigellae (three of them were Sh. flexneri var. Manchester and one Sh. flexneri 2a). These flies contaminated with Shigellae were picked up in a milkshop, a grill-room and in two butcheries.

"5) *Handwashouts.* Out of 195 samples of washouts taken from hands of persons working in food stuff shops, pathogenic enterobacteria were not found.

"6) In enteric epidemics (dysentery, typhoid fever and paratyphoid), the infective agents were discovered three times in the way of transmission. In an epidemic of dysentery in a military unit, Sh. flexneri 2a, the type most frequently found in patients, was isolated from a house fly. In an epidemic of paratyphoid fever in Suva Reka, S. paratyphi B-Taunton type, the same type found in patients in this epidemic, was found in well water, proving the hydric origin of this epidemic. In an epidemic of typhoid fever among the population in Zojici, S. typhi of the same type found in patients in this epidemic, was isolated in the mud in the nearest proximity of the well."

De La Torre, J. A., Olarte, J. & Joachin, Alicia. **Treatment of Shigellosis with Tetracycline in Infants under 2 years of age.** *Pediatrics.* Springfield, Ill. 1959, June, v. 23, No. 6, 1136–42. [16 refs.]

In Mexico City shigellosis is endemic and accounts for 17% of admissions for diarrhoea in children under the age of 2 years who are treated at the Hospital Infantil de Mexico. The authors set out to test clinically the effect of tetracycline in young children suffering from this disease, in contrast to a control group who received similar supportive treatment and a placebo, but no antibiotic. In 92 of the 98 patients *Shigella flexneri* was isolated and in the other 6 *Sh. boydii.*

Isolation was made by the culture of rectal swabs in lactose-methylene-blue agar, SS Difco agar and blood-agar plates, also on tetrathionate-enriched broth. 9 stool cultures were obtained during the period of hospital treatment, the first 3 daily and thereafter every other day.

All patients were placed initially under observation for 60 hours, during which time fluid replacement and dietetic therapy were carried out, in order to eliminate from the trial all those in whom death was inevitable, and to make the critical assessment only when the fluid balance had been restored. Allocation of patients to the experimental and control groups was by random selection and neither nurses nor doctors knew whether tetracycline or a placebo was being administered. Therapy was continued for 7–8 days, tetracycline being given orally in the dose of 50 mgm./kgm./24 hours in 4 equal parts every 6 hours. In 5 patients for the first 2–5 days it was given by intramuscular or intravenous injection at a dosage of 30 mgm./kgm./24 hours. [It seems doubtful if in these children the trial was "blind".] The criterion of bacteriological cure was 3 negative stool cultures, clinical recovery was defined as

the cessation of vomiting and diarrhoea. with normal appetite, while a relapse was diagnosed by the reappearance of symptoms after 7 'days' remission. Death, or lack of response to therapy calling for a change of antibiotic, constituted failure. Severity was assessed by the number of stools passed daily.

At the termination of the observation 59 patients out of 98 remained, of whom 26 were placed in the experimental and 33 in the control group. 60% of these children were under 12 months old. The groups were roughly comparable in age composition, in the average state of nutrition and in initial severity.

Of the 26 children treated with tetracycline, 14 recovered and 12 were failures, of whom 4 died and 8 required a change of therapy. Improvement began between the 3rd and 7th days in most patients. In the control group 11 recovered and 22 failed to do so, of whom 7 died. There were no relapses. In 11 children treated with tetracycline and who recovered, 4 continued to excrete shigellae in their stools, while out of 6 control children who became free from symptoms on the placebo, 4 still had positive stools at the end of the trial period. The authors remark that the action of tetracycline, in those children who benefited from it, was slow. Their numbers were too small to permit statistical analysis, though clinical cure could be recorded in 53·8% of tetracycline-treated patients, but only in 33·3% of the controls.

[It appears to the abstracter that tetracycline compares unfavourably with chloramphenicol in the treatment of infantile shigellosis.] *J. H. Walters*

ZHDANOV, V. M. **Results and Prospects in the Prophylaxis of Dysentery.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 1044–8. [Translated from Russian.]

This is an abridged version of an address (presumably presidential) to an All-Union Congress on the prophylaxis of dysentery. Although it deals largely with medical administrative matters and what can be achieved by the full implementation of governmental instructions already issued it is, for the most part, reasonably sound and balanced. The very large number of publications coming from immunologists in U.S.S.R. and the satellite countries that are concerned with various vaccines designed for the prophylaxis of dysenteric infections are indications of the interest in these conditions and the importance given to their conquest. It is clear, however, that Dr. Zhdanov is fully aware of the achievements in this field and understands the limitations of vaccine prophylaxis; his solutions to the problem of the prevention of dysenteric infections depend on early exact diagnosis, immediate and fully adequate treatment with approved antibiotic combinations coupled with the exhibition of the highest standards of personal hygiene and mass propaganda to emphasize its importance to the general public. He expects no help from bacteriophage preparations and little from immunological procedures that are at present available.

Although there is nothing novel in the recommendation, the discourse does reveal information of considerable interest about the change in frequency of the different bacterial types of shigellae encountered in the U.S.S.R. over the years. In 1930 Shiga dysentery (known as Grigor'ev-Shiga in the U.S.S.R.) accounted for up to 80% of the bacteriologically confirmed cases; through the years, with some fluctuations, the incidence fell gradually until in 1950 Shiga infections were rarely encountered. With the gradual disappearance of Shiga dysentery, however, the relative frequency of the mannite-fermenting dysentery organisms increased and at the present time it would appear that in the U.S.S.R. the distribution of the various antigenic types is not very different from that seen in most other parts of the world.

[Accurate information about the distribution of the dysentery groups of organisms has only become available in recent years although at the time of the 1914–18 war it was known that Shiga dysentery was relatively uncommon in North-West Europe but quite common in South-East Europe and in countries bordering on the Black Sea. Nevertheless bacillary dysentery of the Flexner type was of frequent occurrence, but because it was so often clinically mild, as compared with the Shiga infection, it was not brought to the notice of the authorities in many areas. The almost complete disappearance throughout the world of Shiga dysentery is a remarkable fact, but equally remarkable is the enormous increase in the incidence of Sonne dysentery in all countries, including the U.S.S.R. This organism was first isolated in 1904 (DUVAL, *J. Amer. Med. Ass.*, 1904, v. 43, 381) but for many years was infrequently encountered, even after Sonne's own publication (SONNE, *Giftfattige Dysenteribaciller.* (1914), Copenhagen). In 1927 the present reviewer, investigating acute intestinal conditions in a Child Welfare Centre in Cairo, found that out of some 300 consecutive cases of acute dysentery approximately 15% were due to Shiga's bacillus, 70% to organisms of the Flexner group and only just over 9% to Sonne [see PERRY and BENSTED, *Trop. Dis. Bull.*, 1929, v. 26, 897]. In similar institutions to-day in most parts of the world, certainly in the U.K., bacillary dysentery is almost entirely caused by Sonne's bacillus and it is of particular interest to find that this is also true of many parts of the U.S.S.R.] *H. J. Bensted*

TUBERCULOSIS

KARASU, N. **The Problem of Tuberculosis in Turkey.** *Tubercle.* 1959, Aug., v. 40, No. 4, 275–87, 1 fig.

This article was written at the request of the editor of *Tubercle* on the occasion of the XVth International Tuberculosis Congress of the International Union against Tuberculosis for which Turkey was the host country in 1959.

The Turkish Republic (pop. 24,121,778 in 1955) is situated both in Europe and Asia. Only 28·4% live in the cities but the proportion is increasing. The average density of population is 83·7 per sq. mile.

Very few tuberculin surveys were done before 1950 but by the end of 1958 nearly 20 million persons had been tested with PPD in the BCG campaign. The results show that in 62 of the 63 provinces the reactor rate above the age of 20 was over 70%. In children aged 0–6 years it was 5–10% in 34 provinces, 11–20% in 22

provinces, 21–30% in 6 and 31–40% in 2 provinces. These figures show that contact with the tubercle bacillus starts at very early ages.

There are only 3 mobile mass radiography units in Turkey. Examination of 55,424 persons in 7 provinces in 1954 revealed active pulmonary tuberculosis in 1·2%. The rate of sputum-positive cases varied from 0·39 to 1·3%.

In Ankara open pulmonary tuberculosis was found in 0·38% of 12,476 persons examined, and in another survey of some 78,000 persons active disease was found in 1·69%.

Dependable morbidity figures do not exist. As far as can be ascertained the tuberculosis mortality rate in the cities fell from 150·7 per 100,000 in 1945 to 78·5 in 1955.

Migration plays an important part in the spread of tuberculosis and communications by road, rail and sea are being improved every year with consequent dissemination of infection. During the war there were epidemics of primary tuberculosis among young soldiers. On discharge many of them took the infection back to their villages. The incidence of tuberculosis in prisons is high.

Tuberculin surveys in cattle have shown a low rate of infection (8·12%). Bovine tubercle bacilli accounted for 6·27% of 2,260 strains isolated from human beings. Full information is lacking but it is concluded that bovine tuberculosis is not a very important problem in Turkey.

The Ministry of Health is responsible for tuberculosis control. Notification is compulsory as may also be treatment and segregation. Certain persons such as barbers and workers in food trades must be examined routinely.

There are 65 government and 39 voluntary tuberculosis dispensaries; beds number 11,000 which is only 1 bed per 23 patients with active tuberculosis. The aim is to have 20,000 beds in 5 years. Because of lack of hospital beds the main weapon against tuberculosis at present is BCG vaccination. *H. G. Calwell*

WICKS, C. A. **Trends in the Epidemiology and Treatment of Tuberculosis.** *Canadian J. Pub. Health.* 1959, June, v. 50, No. 6, 240–44.

The author points out that in Canada in the last 20 years mortality from tuberculosis among all races has declined from 55 to 7 per 100,000. At first the fall was gradual but in the period 1951–6 it was rapid, and is now again becoming more gradual.

This makes the mortality rate a poor yardstick of the incidence of tuberculosis. The author then reviews other methods of estimating it. The figures of the first admission rate showed only a slight fall, possibly due to the high admission rate among immigrants. Over the period 1938 to 1957 the number of patients in institutions has fallen from 77·8 to 71·8 per 100,000; it was 111·1 in 1952 but the decrease in length of stay makes this a fallacious figure.

Notifications have fallen from 81·0 to 48·2 per 100,000, but because of different provincial regulations this figure is unsatisfactory. The percentage of positive tuberculin reactions would be a good index but is not available at present and may be invalidated by BCG.

Both the age-sex mortality rates and the first admission rates show the familiar fall in the 10–40 age-group with a rise in the 60+ age-group.

The author then discusses a table showing the results of X-ray screening of selected groups of patients. This gives a range of 214 screened to find a case of active tuberculosis in Homes for Aged and transient cases, 2,381 screened to find 1 case in community surveys, 276 prisoners for 1 case, 305 adult contacts for 1, and 571 for 1 in patients referred by physicians.

The number has risen most dramatically, when 1957 alone is compared with 1946–51, in the physician-referred group—243 to 571—and in the self-referred group, 350 to 833.

The author is not satisfied with any of the yardsticks at present available. *F. H. Young*

CARPENTER, R. G. & STEWART, C. J. **Trial of a Self-Firing Heaf Multiple Puncture Machine.** *Tubercle.* 1959, Aug., v. 40, No. 4, 251–6, 2 figs.

A previous trial [this *Bulletin*, 1958, v. 33, 938] showed that the technique of different workers could give rise to variations in the size of Mantoux [intradernal] and Heaf [multiple puncture] tuberculin reactions. It was concluded that the Heaf test was less affected by the tester than was the Mantoux test.

A Heaf "gun" has now been designed the needles of which are released automatically when the pressure on the plate in contact with the skin reaches 2½ lb.; this was compared with the standard Heaf gun which requires a trigger to be pulled to release the needles.

2 groups of 48 patients in a mental hospital were tested, one male and the other female. The subjects in one group were all given 2 tests with the standard instrument, one being given by each of 2 testers. When these tests were completed all the subjects were immediately tested again with the automatic gun by both testers. The sites were changed at random by presenting the patients in random order. The procedure was repeated 3 days later on the second group of subjects.

7 days after testing the reactions were read by 2 independent observers. A reaction of 3 papules or more was regarded as positive.

The results obtained with the standard instrument showed that the effect of the tester on the size of the reaction had persisted since the previous trial 2 years earlier. It was also seen that the pressure of the end plate on the skin at the moment of release had a decided effect with one tester on the size of the reaction but not with the other tester. The automatic machine did not eliminate differences between testers in the size of reactions produced but it did limit the number of small reactions and is therefore thought to offer greater safeguards against tester error.

Details of the design and analysis of the trial are given in an appendix to the paper. *H. G. Calwell*

TAUBENHAUS, L. J. **The Tuberculin Reaction in Female Hospital Patients.** *New England J. of Med.* 1959, Aug. 13, v. 261, No. 7, 328–30.

In general hospitals routine X-ray examination of all patients admitted has been reported to yield a discovery

rate of tuberculosis several times greater than that obtaining in the surrounding population. Many hospitals, however, will not adopt a policy of routine X-ray examination.

The tuberculin test is an effective screening device for tuberculosis in certain age-groups but it has not been studied extensively in hospital populations. If a sufficient proportion of patients are tuberculin negative the test can serve as an effective screen and eliminate the need to X-ray non-reactors. Any existing tuberculosis could then be discovered by X-raying the reactors only, thus reducing cost and work and radiation exposure.

All patients admitted to a women's surgical hospital in Massachusetts in the 10 months preceding the end of September 1958 were Mantoux tested with 5 TU of OT and all who remained long enough for the tuberculin test to be read are included in this study. It was planned to X-ray all reactors and as a control non-reactors admitted during the second half of the period were X-rayed also.

Of the 1,356 patients tested 397 (30%) reacted (induration over 5 mm. at 44–52 hours—usually 48 hours). The reactor rate was 1% in the age-group under 20. It rose to 27% at 40–49 years and fell to 6% at 70 years and over. Among the positive reactors the older age-group tended to have weaker reactions.

331 patients with positive reactions were X-rayed. Of these 203 (61%) showed no radiological evidence of tuberculosis, 122 (37%) had evidence of inactive tuberculosis and 6 (2%) had evidence of active tuberculosis. All in the last category were aged 20–49 years which agrees with the general impression that tuberculosis in women occurs primarily in those of childbearing ages. There was no relation between the degree of tuberculin sensitivity and the X-ray findings.

There was no radiological evidence of active pulmonary tuberculosis in the 233 non-reactor patients but 42 (18%) had small hilar calcifications or scars. These could have been cases of completely healed childhood tuberculosis or histoplasmosis.

On the basis of these findings it was concluded that the Mantoux test is an effective method for screening female surgical patients in Massachusetts.

H. G. Calwell

KREBS, A. Über die Aussichten, eine Mischinfektion mit humanen und bovinen Tuberkelbakterien zu erkennen. **[On the Diagnostic Possibilities in Double Infections with Human and Bovine Tubercle Bacilli]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 422–32. [22 refs.]

Attention is drawn to a case of pulmonary tuberculosis in which numerous cultures were made and guinea-pigs and rabbits were injected. The bovine infection would have been missed entirely in the culture media but was revealed in the subcultures from the tissues of both the guinea-pig and rabbit.

Experimental observations on artificial mixtures of bovine and human tubercle strains in varying proportions strengthen the conclusion that the presence of mixed bovine and human infection in clinical cases may be readily missed if the observer depends entirely on cultural results.

J. W. McLeod

PACY, H. **Thiacetazone and the Erythrocyte Sedimentation Rate in Tuberculosis.** *Med. J. Australia.* 1959, May 23, v. 1, No. 21, 703–6.

The erythrocyte sedimentation rate is generally considered as an important criterion of activity in pulmonary tuberculosis, but it has fallacies. H. MALLUCHE (*Ärztl. Forsching*, 1950, v. 4, 99) showed that the erythrocyte sedimentation rate was altered by the thiacetazone treatment of the disease.

This paper studies this finding by a series of experiments. In a normal patient's blood the erythrocyte sedimentation rate (Westergren method, measured in mm. at 1 hour and 2 hours) fell from 2/3 (without thiacetazone) to 1/2 (when 1 drop of 10% thiacetazone solution was added to 2 ml. citrated blood), but in 6 tuberculous patients the fall was much diminished in similar experiments, *e.g.*, 56/95 to 2/6, and 101/121 to 2/5 in 2 patients with progressive tuberculosis. This effect was not produced by PAS, streptomycin or penicillin.

The effect was not produced when the concentration of the drop of thiacetazone solution was reduced to 1%. A further experiment showed that an appreciable effect appeared when the concentration reached 1 drop of 8% solution, but even with the 10% solution the effect gradually wore off when the tubes were read hourly, until at the end of 12 hours the effect was very slight. The slowing effect was still produced when the 10% thiacetazone solution was added to the citrated blood at varying intervals up to 12 hours.

The slowing effect of the borderline concentration on the blood of patients with active tuberculosis is variable and not related to the erythrocyte sedimentation rate. The average fall of erythrocyte sedimentation rate in 53 tuberculous patients treated for 6 weeks with 50–100 mgm. per day of thiacetazone when compared with that in 291 tuberculous patients under other treatment did not show any constant difference.

Malluche's results were thus confirmed, but his assumption that a change in the plasma was the cause of the gradual diminution of the thiacetazone effect is not confirmed. The author thinks that the thiacetazone is unstable in dilutions below 10%, and its disintegration causes the effect to disappear.

Practically, a dramatic fall in the erythrocyte sedimentration rate indicates that the therapeutic concentration in the blood is effective. The author suggests that frequent administration of the drug may produce a higher effective concentration than the less frequent administration of higher doses. The inconclusive effects noted in tuberculous patients suggest that in many cases the effective concentration of the drug in the blood is not reached.

F. H. Young

NISHIHARA, H., FROMAN, S. & WEIMER, H. E. **Serial Determinations of Serum Glycoproteins and Proteins in the Early Stages of Experimental Tuberculosis.** *J. Lab. & Clin. Med.* 1959, Aug., v. 54, No. 2, 257–61. [11 refs.]

"The systemic effects of acute experimental tuberculosis as reflected by alterations in the concentration and distribution of the serum glycoprotein and proteins have

been investigated in adult female guineapigs. The levels of the protein-bound carbohydrates and proteins in serum and in the seromucoid, albumin, and globulin fractions were determined in groups of animals sacrificed 8, 15, 19, 29, and 50 days following inoculation with 0·1 mg. *Mycobacterium tuberculosis*, strain B88. The results demonstrate that the acute infection is characterized by the following changes: (1) significant and rapid increases in the components of the seromucoid and globulin fractions; (2) rapid decline in the protein components of the albumin fraction; (3) no change in albumin polysaccharide values; (4) more pronounced changes in the protein components of the serum subfractions in the initial stage of the infection; and (5) stability of the serum glycoprotein pattern after 15 days' infection notwithstanding progressive spread of disease."

BOESAART, J. W. Een geval van placenta-tuberculose. [**Tuberculosis of the Placenta**] *Nederl. Tijdschr. v. Geneesk.* 1959, Sept. 12, v. 103, No. 37, 1849–52, 2 figs. [16 refs.]

The English summary appended to the paper is as follows:—

"A tertipara, aged 27, with a history of pulmonary tuberculosis which treatment had cured, was given tuberculostatics prophylactically in the last month of pregnancy. An undisturbed pregnancy terminated in the spontaneous birth of a girl weighing 3890 grammes; the confinement was normal. Microscopic evidence of tuberculosis was found in the placenta, which looked normal to the naked eye. Mother and child are both healthy to date."

MITCHELL, R. S. & AUERBACH, O. **Surgery in Pulmonary Tuberculosis. A Review.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 207–15. [115 refs.]

See also p. 1262, RAMSAY & PINES, **Results of Treatment of Pneumoconiosis complicated by Tuberculosis.**

SARKOV, T. V. La lutte contre la tuberculose dans la R.P. Bulgarie. [**The Anti-Tuberculosis Campaign in Bulgaria**] *Santé Publique.* Bucharest. 1958, v. 1, No. 2, 75–88, 10 figs. (2 on pl.)

The population of the People's Republic of Bulgaria is about 7,664,000 of whom some 2,466,000 live in towns or cities and the remainder in rural areas. There is on average one tuberculosis dispensary per 68,500 inhabitants. The tuberculosis service on its present scale is of fairly recent creation, having grown from 17 health centres without beds in 1939 to almost 7 times that size.

The total number of beds in hospitals and sanatoria is 9,760 and in preventoria 3,099. The number of beds is insufficient and there is in addition a service of domiciliary treatment.

Where the tuberculosis dispensary functions satisfactorily the discovery rate by mass radiography is relatively low but where it functions badly the discovery rate is high. About 5–10% of new cases are found by mass radiography, 80–90% by general physicians and the remainder at tuberculosis dispensaries, especially by the examination of contacts.

Mass radiography can cover only about 15–20% of the population in one year; it must therefore be directed at the most vulnerable section and is of the utmost value in rural areas where access to clinics is difficult and particularly for elderly persons.

The tuberculosis mortality rate in the area served by the tuberculosis Institute fell from 94·6 per 100,000 in 1946 to 7·8 in 1956 and the number of notified cases from 1,270 to 1,031.

BCG vaccination was used only on a small scale until after 1950; it was then extended. Newborn infants are vaccinated orally and all other persons subcutaneously [*sic*]. More than 2,500,000 vaccinations and revaccinations have now been done with satisfactory results. A favourable influence on tuberculosis mortality of infants has been seen. Danish vaccine was used until 1954 and then replaced by Soviet vaccine because of a 2–3% incidence of lymphadenitis in those vaccinated orally. *H. G. Calwell*

SHORT, G. M. **BCG Vaccination and the Depot Tuberculin Test.** *Tubercle.* 1959, Aug., v. 40, No. 4, 271–4.

In 1955 a policy of tuberculin testing and BCG vaccination was introduced for students in the University College of East Africa, Uganda. In 1957, in order to reduce the number of visits in connexion with vaccination it was decided to investigate the depot tuberculin test as described by JAMES and PEPYS [this *Bulletin*, 1956, v. 31, 805] and at the same time to determine how soon after vaccination with a British freeze-dried vaccine tuberculin conversion occurs.

180 students entering college, not previously tested or vaccinated, were tested with PPD by the Heaf method. The tests were read at 72 hours and of the 27 non-reactors 24 were vaccinated intracutaneously with freshly reconstituted dried vaccine made by the Glaxo Laboratories, England.

The PPD used for the pre-vaccinal test (2 mgm./ml. containing 10% glycerol) was diluted and added to liquid paraffin (8 parts) and lanolin (1 part) to prepare depot tuberculin of which the intracutaneous test dose of 0·05 ml. contained 5 TU. The vehicle itself was used for control tests in the same amount.

11 days after vaccination 19 of the vaccinated students were given intracutaneous injections of the depot tuberculin and the vehicle 2 inches apart. They were instructed to report when they noticed any swelling at the test sites.

18 students reported at varying times: the first 13 days after vaccination and the last 22 days after vaccination. All showed induration and erythema at the depot tuberculin site and none at the control site. When seen again 56 days after testing there were visible and palpable swellings at both sites but in all cases the control reaction was the smaller. In 3 there was no reaction to the control injection.

On examination 6 months after testing the tuberculin reactions were still larger than the controls except in

1 student in whom they were equal. An additional student, who had not previously been seen, conformed to the general pattern, and another stated that his reactions had increased in size since the previous examination.

When examined 13 months after testing all still showed reactions at the test site and most at the control site. Some reactions had increased in size at both sites. The persistent reactions caused no physical or mental distress..

It was concluded that the depot tuberculin test is an effective and acceptable indicator, in the African, of tuberculin conversion. It was also concluded that the rapidity and thoroughness of tuberculin conversion with Glaxo freeze-dried vaccine is probably as good as with fresh liquid vaccine. *H. G. Calwell*

PRINSLEY, D. M. & DROLLER, H. **Tuberculin Reactions and B.C.G. Vaccination in Old Age.** *Brit. J. Dis. Chest.* 1959, July, v. 53, No. 3, 296–301. [20 refs.]

Pulmonary tuberculosis is common in elderly men some of whom appear to be suffering from acute disease of recent origin. One of the factors in the incidence of acute disease in the elderly may be the fresh infection of a tuberculin-negative subject.

In order to discover the incidence of tuberculin anergy among the elderly in Yorkshire (England) a tuberculin survey was made on a large number of male and female patients in geriatric wards. In addition a group of non-reactors who were thought to be exposed to possible risk of tuberculous infection were vaccinated with BCG. This paper describes the results of the survey of 1,000 elderly patients and the results of vaccination of 101 non-reactors.

The Heaf test at 2 mm. skin penetration was used with PPD; all tests were read at 72 hours. The results were:

Age-groups	60–64	65–69	70–74	75–79	80–84	85–89	over 90
Tested	63	111	166	260	233	127	42
% reactors	84	74	71	69	67	69	76

There was no significant variation in the reactor rates over the age of 65 in the different age-groups or between the sexes. However, there was variation when compared with the population densities of the areas from which the patients had come (rural and residential, 57%; highly industrialized city, 75%).

A record was made of the main diagnosis of each patient tested, and the results of the tuberculin test in 7 diagnostic groups showed little variation. No patient was excluded because of severe illness and only those known to have pulmonary tuberculosis and the dying were excluded.

It was felt that ambulant geriatric patients in sanatoria and hospitals containing infectious tuberculous patients were at special risk, and 101 such patients were vaccinated with BCG. 28 received fresh Danish and 73 British freeze-dried vaccine.

In the group of 28 there were 7 accelerated reactions such as can occur in a person whose tuberculin skin test has been negative because of waning allergy; in the group of 73 there were 8 accelerated reactions. There were no severe local reactions. The freeze-dried vaccine produced milder lesions than the fresh vaccine. The conversion rate 3 months after vaccination was 100% with fresh and 92% with dried vaccine. 3 patients vaccinated with dried vaccine did not undergo conversion. The procedure was found to be safe and is considered a worthwhile protective measure for the elderly contact of tuberculosis. [See also this *Bulletin*, 1958, v. 33, 832.] *H. G. Calwell*

HARTSTON, W. **Uncommon Skin Reactions after BCG Vaccination.** *Tubercle.* 1959, Aug., v. 40, No. 4, 265–70, 21 figs. (18 coloured on 2 pls.).

Practitioners of BCG vaccination who read this paper will be greatly in the author's debt. Manifestations of skin disease due to many causes are common in children and when they occur in a child who has lately been vaccinated with BCG are likely to be attributed by parents and family doctors alike to the vaccination. It is therefore most helpful to have such an informative study of the matter, especially one so lavishly illustrated by coloured photographs.

After a description of the normal reaction to BCG vaccination by intracutaneous injection with 0·1 ml. of fresh vaccine (0·075 mgm. of bacilli) the accelerated reaction which occurs in persons who are sensitive to tuberculin is described. These are familiar to all. Hartston mentions in passing that resuspended vaccine from a freeze-dried preparation gives just the same types of reaction as fresh fluid vaccine of the same strength.

The author has vaccinated many children having such skin conditions as xeroderma, ichthyosis, prurigo, eczema, dermatographia and psoriasis. When the site of the inoculation of the vaccine was healthy no abnormal reaction was seen. Diabetic persons too have reacted normally.

The intensity and duration of the local BCG lesion depend on the potency and dose of the vaccine, its homogeneity and the idiosyncrasy of the patient's tissues. The site of injection also makes some difference; for example, reactions are more marked after vaccination into the skin of the upper thigh than into the skin of the upper arm.

Severe acute inflammatory reactions of the skin associated with but not due to BCG include impetigo, eczema due to imprisonment of discharge by a tight dressing or by adhesive plaster; irritation by dry gauze applied too long or too strong antiseptics may produce granulations. Individuals who react to certain tissue-damaging agents with a "sarcoid" pattern of inflammation have been reported to react similarly to BCG vaccination.

Acute skin reactions due to BCG include lymphangitis, ulceration due to deep injection or auto-inoculation. All ulcerated lesions improve by treatment locally with 2½% cortisone ointment. Abscesses in the skin are due to deep injection or secondary infection. Hartston has seen only 6 in 80,000 schoolchildren vaccinated in London. Regional gland abscesses also occur—most commonly in young infants.

Chronic inflammatory reactions include granulomata due to irritant dressings or idiosyncrasy. Daily treatment with 2½% cortisone cream promotes healing and prevents keloid formation.

Lupus may occur. The Medical Research Council trial [this *Bulletin*, 1956, v. 31, 621] disclosed no such occurrence in 14,100 children vaccinated with BCG but in Hartston's experience persistent lupus-type reaction may occur in one person per 3,000 vaccinated. He has collected 20 cases seen 6–12 months after vaccination. All the lesions showed the characteristic apple-jelly areas. Spontaneous healing occurred within 1 year of discovery in every case. If treatment is necessary isoniazid alone (4 mgm./kgm. daily) is recommended.

A unique case of histiocytoma was diagnosed among 70,000 vaccinated schoolchildren in London examined 1 year after vaccination. Full details are given including photomicrographs. Chemotherapy and cortisone were without effect and the lesion was finally excised. The morbid process at work is not understood.

Any of the peculiarities of scar tissue formed in the healing of any skin lesion may occur including keloids, dilatation of capillaries and cavernous naevus.

Transient urticaria may appear within a few days of vaccination and Hartston has seen erythema nodosum once. The Medical Research Council trial discovered 2 cases occurring 4 weeks after vaccination. Among the 80,000 London children vaccinated there were 2 cases of a sparse generalized eruption appearing about 10 days after vaccination. The eruptions closely resembled lupus miliaris disseminatus faciei and healed without scarring. *H. G. Calwell*

Ellman, P. & Andrews, L. G. **B.C.G. Vaccination—a Preliminary Communication.** *Brit. J. Dis. Chest.* 1959, July, v. 53, No. 3, 302–7. [28 refs.]

This paper deals with the follow-up of 264 of the 1,000 persons vaccinated with fresh Danish BCG vaccine since 1950 in the practice of a London chest clinic. The series comprised Heaf-negative contacts of tuberculous persons, newborn infants in tuberculous families and individuals who had requested vaccination. The period of follow-up was 5–8 years.

Details of the tuberculin state of 258 persons are given and show the years during which the Heaf test or the Mantoux test with 5 TU remained positive:

Years	8	7	6	5	
No. of persons	13	82	98	65	Total—258

In one case (child aged 11 years) post-vaccinal tuberculin conversion did not occur but it did so after subsequent vaccination. [No times are mentioned.] 6 patients had to be revaccinated, 2 after 2 years, 3 after 3 years and 1 after 5 years. Thus in 97·7% tuberculin sensitivity endured for a period of 5–8 years. This high figure may have been due to the fact that 36% of the patients had close contact with known infectors, and no segregation was carried out after post-vaccinal conversion had been demonstrated.

A primary tuberculous complex of the lung was found in one child, a contact of his father who had open pulmonary tuberculosis. A postscript to the paper records the finding of active pulmonary tuberculosis in 1959 in a girl who was vaccinated in 1950. She was known to be tuberculin positive in 1952 after which she refused to cooperate further and was excluded from the survey. Her state of sensitivity before the onset of the tuberculosis is therefore unknown. Assuming it to be positive, the known incidence of tuberculosis in the series is 0·77%. *H. G. Calwell*

Comstock, G. W. & Merrell, Margaret. **The Life Table Method applied to the Results of a Trial of BCG Vaccination in Algiers.** *Arch. Inst. Pasteur d'Algérie.* 1958, Sept., v. 36, No. 3, 304–11, 1 fig.

This paper presents, in the form of life tables, the mortality (from all causes) in the vaccinated and non-vaccinated population groups in a controlled trial of oral BCG vaccination of more than 40,000 newborn infants in Algiers [this *Bulletin*, 1954, v. 29, 1147; 1957, v. 32, 569]. Essentially the life table method consists in determining the probabilities of dying from one age to another, and from these, the probability of surviving any given interval of time.

The general pattern of survival was similar for the 2 population groups, each showing a high initial mortality which became progressively less during the 7 years of observation. The advantage of the vaccinated over the unvaccinated group became progressively greater each year: at the end of 7 years 69·3% of the vaccinated group had survived, compared with 65·2% of the non-vaccinated group.

[The authors are concerned solely with illustrating the application of the life table technique to basic data which have already been presented in another, also valid, way; they do not comment on the findings of the trial.] *Ian Sutherland*

Barclay, W. R. **BCG Vaccination.** *Pediatrics.* Springfield, Ill. 1959, Sept., v. 24, No. 3, 478–81.

A review of some of the most important critical trials.

VENEREAL DISEASES

Chaves, A. R. A evolução das doenças venéreas. [**The Evolution of Venereal Diseases**] *Gaz. Méd. Portuguesa.* 1959, Mar.–Apr., v. 12, No. 2, 231–41. [12 refs.]

The English summary appended to the paper is as follows:—

"The study of statistics, both in Portugal and other countries, concerning venereal diseases, shows a marked decrease in these diseases. The examination of each of them permits to verify that although blennorrhagia has very much decreased, it was however the most rebellious of all, and that syphilis decreased about 80–90%, in comparison with the figures observed ten years ago. This fact is not only due to the efficiency and easy application of antibiotics, but also to improved methods of diagnosis and also to better prophylactic measures.

"Nevertheless, the use of all prophylactic methods within our reach, to combat those diseases, should not be neglected."

LEVY, B. **Scrub Typhus in the Differential Diagnosis of Venereal Disease.** *J. Roy. Army Med. Corps.* 1959, July, v. 105, No. 3, 125–7.

"Two cases of scrub typhus are described. In both the existence of a genital eschar with regional adenitis pointed to a venereal infection. Although only two cases have been recorded during the previous two years at the Venereal Disease Department of the British Military Hospital, Singapore, it is possible that others have been missed and it is considered that scrub typhus should enter into the differential diagnosis of certain types of genital ulcers, particularly those occurring in soldiers serving in areas where scrub typhus is endemic."

SIMPSON, W. G., MATTHIS, A. W., HARRIS, A. & PRICE, Eleanor V. **Evaluation of the Rapid Plasma Reagin Test in Field Operation.** *Pub. Health Rep.* Wash. 1959, June, v. 74, No. 6, 473–7, 2 figs.

The fact that the rapid plasma reagin test (RPR) can be carried out in 18 minutes, and results can be reported after 40 minutes, suggested that it might be valuable in testing immigrant Mexican labourers in the U.S.A.

This test was carried out on 47,579 sera and the reactivity rate was 9·7%; a selected group of 1,672 sera were submitted to the following tests in parallel with these results: percentage non-reactive RPR 45·8, TPCF 35·5, Kolmer cardiolipin 48·4, Hinton 49·6, VDRL 55·7. When 1,604 specimens giving definite results to all tests were compared the relative agreement rates with RPR were: Kolmer 91·4%, Hinton 90·3%, VDRL 80·7% and TPCF 67·8%.

A large number of statistics are given in 3 tables and 2 figures; what seems to emerge is that the RPR test is very suitable as a screen test where rapid results are essential; incidentally it appears that the TPCF is oversensitive and therefore unreliable, but this has nothing to do with the purpose of this paper.

T. E. Osmond

BROWN, W. J. & BUNCH, W. L., Jr. **How Good is the Reiter Protein Complement Fixation Test for Syphilis?** *Southern Med. J.* 1959, July, v. 52, No. 7, 783–7, 5 figs.

These authors compared the Kolmer Reiter Protein complement-fixation test (KRP) with the TPI and VDRL slide tests by testing a number of sera in parallel. In 130 sera from untreated primary syphilis the KRP was reactive or weakly reactive in 64%, the TPI in 41% and the VDRL in 66%; the corresponding figures in untreated secondary syphilis were 98, 96 and 100%; in treated early syphilis the figures were 45, 41 and 13% and in treated late syphilis 90, 96 and 85%. In syphilis untreated or treated with heavy metal only the figures were 48, 95 and 46%; in those treated with less than 12 injections of arsenicals the figures were 18, 10 and 87%.

In sera from persons presumed normal KRP and TPI gave 3% and 8% reactions and VDRL none; in those from patients with diseases other than syphilis the figures were 12, 7 and 6% and in leprosy 5, 0 and 27%.

In biologically false positive reactors, (a) in those who had previously given negative TPI reactions the figures were 8·6, 4 and 48% and (b) in those diagnosed clinically 35, 34 and 44%.

Thus it appears that KRP becomes positive nearly as early as VDRL but remains reactive longer; it closely parallels the TPI test in all types of non-syphilitic sera. [KRP seems to lack specificity in diseases other than syphilis compared with TPI and VDRL.]

T. E. Osmond

RINTELEN, F. Zur Prophylaxe der Neugeborenenblennorrhoe. [**Prevention of Gonorrhoea in the Newborn**] *Bull. Schweiz. Akad. Med. Wiss.* 1959, May, v. 15, Nos. 2/3, 135–43. Discussion 143–4.

This paper begins with a facsimile of the beginning of Credé's paper published in 1880 recommending the application of silver nitrate solution for the prevention of conjunctivitis in the newborn. The author has made enquiries about methods in use at the present day, and obtained information from 9 centres in Switzerland, 9 in Germany, 5 in France and 10 in other European countries. The majority use some silver preparation, 6 use penicillin, 1 "ophtopen", 1 zinc sulphate and 1 nothing. He considers that silver salts are too irritating, colloidal silver preparations not sufficiently bactericidal, and that penicillin should be avoided because of the danger of producing bacterial resistance. [Bacteria acquire resistance to penicillin so slowly, if at all, that this danger, from a single application, is non-existent, and this argument is therefore baseless.] He advocates the use of a quaternary ammonium compound, Desogen (0·5% of the "non-perfumed original solution"): this has been successfully applied to the eyes of 310 babies in his clinic at Basle. Particulars are given of its capacity to inhibit growth *in vitro* of 5 pathogenic organisms, and some observations were made on its persistence in the conjunctival sac: in 14 adults it was still detectable after 3 minutes but after 5 it had disappeared from all but 2. [Some further experiments were apparently done of which the results are given in Table 4, but the heading of this is non-exp'anatory and the text includes no reference to it.] It is not known whether Desogen acts on viruses, but this is being investigated. A discussion of this paper follows: the principal contributions refer to the mode of action of Desogen on the bacterial cell, and to the use of this disinfectant for the storage of syringes.

L. P. Garrod

ELLIS, F. A. & BERESTON, E. S. **Reiter's Syndrome Versus Keratosis Blennorrhagica Sine Blennorrhea.** *Southern Med. J.* 1959, July, v. 52, No. 7, 828–33, 1 fig. [10 refs.] Discussion 833–4.

These authors hold the view that so called keratodermia blenorrhagica is not caused by gonorrhoea [as

is generally agreed today] but by some other infection(s), and is often associated with Reiter's disease; moreover the typical lesion is a parakeratosis rather than a keratosis. They describe 3 cases in support.

The first showed a non-gonococcal urethral discharge, conjunctivitis and arthritis; in hospital, paronychia of fingers and toes developed together with hyperkeratotic lesions of many areas especially the soles and right palm; 4 years later he had a relapse similar to the original attack. The second patient showed multiple arthritis, conjunctivitis, scaling of the scalp and paronychia [but no mention is made of urethritis]. The third patient showed a typical Reiter's syndrome (but without conjunctivitis) with crusted lesions on the extremities but was diagnosed as staphylococcal septicaemia. Histopathology revealed inflammatory cells and nuclei extending into the keratin layer of the skin and a decrease of the granular layer below, oedema of the epidermis, acanthosis with long dermal pegs with dilated capillaries resembling hypertrophic psoriasis.

Treatment of this condition is unsatisfactory but cortisone is of value in relieving the arthritis and the disease is essentially self limiting.

1 figure shows a section of the skin illustrating the points described. *T. E. Osmond*

Montgomery, M. M., Poske, R. M., Barton, E. M., Foxworthy, D. T. & Baker, L. A. **The Mucocutaneous Lesions of Reiter's Syndrome.** *Ann. Intern. Med.* 1959, July, v. 51, No. 1, 99–109, 6 figs.

To the triad of urethritis, conjunctivitis and arthritis these authors propose to add mucocutaneous lesions. After quoting several authors who have reported these last named in a few cases they give an account of 38 patients with Reiter's disease, 80% of whom exhibited such lesions as balanitis circinata, perimeatal erosions, macules and erosions of the oral and pharyngeal mucosa, cutaneous lesions, mostly of the keratodermia blenorrhagica type and keratosis of the finger and toe nails.

Lesions on the penis, keratodermia of the sole of the foot and nail changes are beautifully shown in 4 figures and 2 tables set out details and location of oral and pharyngeal lesions and cutaneous lesions respectively; 1 figure shows the microscopic picture of a cutaneous lesion demonstrating elongation of the papillae with cellular infiltration and oedema of the connective tissue. Incidentally adrenocorticotrophin and corticosteroids had no effect on skin lesions.

It has long been recognized that keratodermia blenorrhagica was probably not caused by the gonococcus but the other mucocutaneous lesions described in this article are not so well known. *T. E. Osmond*

Oates, J. K. & Hancock, J. A. H. **Neurological Symptoms and Lesions occurring in the Course of Reiter's Disease.** *Amer. J. Med. Sci.* 1959, July, v. 238, No. 1, 79–84.

These authors report in detail three patients suffering from Reiter's disease who gave evidence of neurological involvement.

The first developed gonorrhoea after homosexual exposure; the urethritis was followed by conjunctivitis, keratodermia of the glans penis and arthritis; he was treated with penicillin, tetracycline and also phenybutazole (200 mgm. twice daily) to relieve pain; later he developed paranoid delusions followed by epileptiform convulsions; the leucocyte count rose to 10,000 and the cerebrospinal fluid was found to contain 29 cells per cmm. and 250 mgm. protein per 100 ml. He gradually improved and was discharged after about 7 weeks in hospital.

The second patient was admitted for low back pain; on examination he showed conjunctivitis, urethral discharge, circinate balanitis and swelling of the Tendo Achillis; later he developed arthritis of several joints with weakness of both arms presumably due to an affection of the fifth cervical segment. Various pathological tests were mostly negative and a diagnosis of peripheral neuropathy was made. Wasting of the arm muscles persisted for at least 3 months.

The third patient apparently contracted gonorrhoea and non-gonococcal urethritis at the same time; severe pain in the back was diagnosed as radiculitis and this was followed by multiple arthritis, keratodermic lesions of the feet and conjunctivitis. He also complained of severe pain in various places including the back (6th dorsal spine), left groin and left thigh.

The authors conclude that the first case was one of meningoencephalitis, the second neuritis and the third of root pain, all associated with Reiter's disease.

T. E. Osmond

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases.

Smythe, P. M. & Bull, A. **Treatment of Tetanus Neonatorum with Intermittent Positive-Pressure Respiration.** *Brit. Med. J.* 1959, Aug. 1, 107–13, 3 figs.

10 infants, the oldest being 14 days old, suffering from tetanus were treated with tracheotomy and intermittent positive pressure ventilation: 3 survived and there was evidence in 2 others that the infant would have recovered from tetanus but for other factors such as septicaemia. Mephenesin in doses of 33–130 mgm. an hour by stomach tube, or tubocurarine 10 mgm. given intramuscularly with hyalase were used to control spasm, the latter being more effective. Though the mortality is still high, it is better than with earlier forms of treatment and the authors feel the method must be tried further and the details of management improved. [Full case histories and a long discussion of the special difficulties in using this method in neonates are given. It should be studied by all who may have to tackle this clinical problem.] *A. B. Christie*

LAWRENCE, J. R. & SANDO, M. J. W. **Treatment of Severe Tetanus.** *Brit. Med. J.* 1959, Aug. 1, 113–18, 2 figs. [Numerous refs.]

9 patients suffering from severe tetanus were treated with tubocurarine, tracheotomy and artificial ventilation. 4 patients died, 2 from pulmonary embolism and 1 from renal failure. The difficulties of the method are fully discussed and the authors feel that, with all its complications, the method saves lives that would otherwise be lost. It is indicated in fulminating cases and in severe cases where sedation fails.

A. B. Christie

ECKMANN, L. Die gleichzeitige Anwendung von Serum und Toxoid in der Tetanusprophylaxe. [**Simultaneous Use of Serum and Toxoid in the Prophylaxis of Tetanus**] *Schweiz. med. Woch.* 1959, Mar. 21, v. 89, No. 12, 311–15. [27 refs.]

There is considerable persistence of tetanus, a disease as exacting to the medical attendant as it is formidable to the patient, and marked divergence of opinion exists about the value of combined active and passive immunization in prophylaxis. In view of these facts a careful and extensive investigation of the immunity resulting from this form of prophylaxis has been carried out.

700 persons have been examined and in all 3,000 determinations made of the levels of antitoxin in their sera.

The results obtained support very strongly the practice of administering toxoid in all cases since without exception the individuals who had had such treatment even 6 or 7 years earlier showed a vigorous response to a " booster " dose.

A scheme of procedure for dealing with severely wounded persons according to their state of immunity is suggested.

1. Immune persons, *i.e.* those who have had more than one dose of toxoid at intervals of 20 days in the previous 6 months or 3 doses in the previous 12 months.

Such persons may be left untreated or given 1 cc. of toxoid.

2. Non-immune persons, *i.e.* all others than those in category 1.

(a) Persons adequately immunized more than one year before the injury under treatment. For these a booster dose is essential.

(b) Those inadequately immunized in previous years should receive immediately one injection of toxoid, possibly associated with 1,000 antitoxic units of serum and followed at 12 weeks by a further dose of toxoid.

(c) If never immunized they should get the same administration of toxoid and 3,000 units antitoxin in separate areas of body and administered with separate syringes. Further doses of toxoid should be given at 4 weeks and 3 months.

(d) The last case to be considered is the person never immunized for tetanus who has had a previous dose of some other antiserum.

For such, in addition to toxoid, 6,000 units of antitoxin is suggested provided that the wound is of such a character that the risk associated with large doses of serum must be taken; only early administration of serum is justified, *i.e.* within 24 hours of wounding.

J. W. McLeod

CHERRICK, G. R., POTHIER, Lillian, DUFOUR, J. J. & SHERLOCK, Sheila. **Immunologic Response to Tetanus Toxoid Inoculation in Patients with Hepatic Cirrhosis.** *New England J. of Med.* 1959, Aug. 13, v. 261, No. 7, 340–42. [15 refs.]

" Twenty-eight patients with hepatic cirrhosis and 22 subjects without cirrhosis were given immunizing doses of tetanus toxoid. The antibody response in the two groups did not differ significantly.

" No significant difference was found in the antibody response of 10 patients with hepatic cirrhosis as compared with the response of 9 noncirrhotic subjects to a booster dose of tetanus toxoid."

[The work was done in London.]

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

GIORN. DI MALATTIE INFETTIVE E PARASSIT. 1959, June, v. 11, No. 6, 392–448. [Numerous refs.] Simposio sulla brucellosi (Bologna 5–6 Dicembre 1958). [**Symposium on Brucellosis**]

Under the auspices of the Italian Society for the Study of Infectious and Parasitic Diseases a symposium on brucellosis was held at Bologna on 5–6 December 1958.

The 2 main themes were laboratory diagnosis in ruminants and diagnosis, especially as regards " chronic " brucellosis, in man.

S. PALTRINIERI and P. BIGGI gave 2 papers (pp. 392–404 and 404–11) dealing with the disease in ruminants with a number of extremely important practical points, among which were that in bovines blood-cultures should be made with much larger amounts of blood than usual—not less than 2 samples of 50 ml. each—; the organisms rapidly localize in the udder and can remain there more or less permanently; cows with an agglutinin titre of 1 in 40 can be considered infected, but agglutination is often negative especially in sheep. The use of 5% NaCl in the test has been helpful, but blocking antibodies are often present especially in sheep. Renoux's coloured antigen has been useful. The ring test is not so satisfactory in sheep as in bovines. Isolation of the organism from bedding is possible. The old concept that non-gravid cows do not contract the infection is wrong, and in goats infection can persist in a flock, from infected kids.

In man, R. Davoli (pp. 411–12) dealing with laboratory diagnosis stated that for blood cultures the centrifuged deposit of haemolysed blood is best; no decision can be given on the result of one agglutination test, and in doubtful cases especially those with very low titres the Coombs test should be used; the persistence of complement-fixing antibodies may be of great importance in the diagnosis of "chronic" brucellosis.

G. Buonomini and Gabbrielli (pp. 413–14) had never had any cases which they could consider as chronic *ab initio*. They had tested 107 definite brucellosis patients after 2–8 years from the end of treatment and had found that 64 still had titres of 1 in 40 or more and 31 others had a positive Coombs test. Intradermal tests were also positive in a high percentage, and they considered that this test can remain positive for a very long time especially if the patient resides in an endemic area. G. Gargani (pp. 415–18) mentioned that between 1948 and 1958 out of 384 blood-cultures 105 were positive, in 3 not till the 35th day; sternal puncture may be valuable when blood culture is negative; non-specific agglutinins are rare but blocking antibodies are present in a number of cases; in the Coombs test the titre should be reasonably high as incomplete antibodies may be present in low titre in healthy persons; a few positives can only be detected by the complement-fixation test.

V. Chini (pp. 419–22) suggested that chronic brucellosis can assume different aspects in different regions of the world; the use of melitin in diagnosis is valuable if accompanied by a generalized reaction, as is also fever after intravenous injection of small amounts of brucella vaccine; the possibility of the disease should be borne in mind in all subjects with a long-continued history of ill health with slight febrile attacks; in the rheumatism-like form the joint symptoms are generally less than in rheumatoid arthritis; muscle biopsy may be helpful. S. De Renzi and G. Cave Bondi (pp. 423–40) are firmly convinced there is a chronic form which they define as lasting for more than 1 year and for which organisms in the R phase (relatively attenuated) may be responsible. 1 of their patients had symptoms [associated with pulmonary tuberculosis for part of the time] for 24 years, being finally proved positive after splenic puncture and culture of the pulp. If *Br. melitensis* is isolated (on modified Petragnani medium) a splenomegalic, and an anaemic-febricular form can be found; the spleen condition may become irreversible, giving rise to a Banti-like condition; minor forms of purpura are frequent; in addition to melitin, the increase in fever which occurs after splenic contraction induced by adrenaline or by spraying ethyl chloride on the skin of the left upper quadrant of the abdomen are useful in diagnosis. For treatment intravenous brucella vaccine in doses of 25–1,500 million at intervals of 5–6 days is good but probably best in the chronic form; chlortetracycline 1·5 gm. each day for not less than 70–80 days, and prednisone 15 mgm. each day which should be replaced by corticotrophin when the patient becomes apyretic. The reappearance of eosinophils may be an indication of improvement. G. T. Sicca (pp. 441–3) considered that chronic brucellosis is not a condition *per se* as even in cured patients it is still possible to find signs of the previous infection and the intradermal reaction is positive in the great majority. F. Colonnello (pp. 444–7) gave some illustrative clinical cases including one remarkable case where brucella was isolated from the pus from a left chronic otitis media of several years' duration; he considered that in a case of pyrexia if the intradermal test was negative this was definitely against brucellosis. Antibiotic treatment limited to the febrile period only is very largely to blame for the disease becoming chronic, though he found that relapses occurred or the disease had become chronic in a number of properly treated cases.

A summary of the conclusions of the symposium suggests that (1) in animals the disease may vary according to whether the animal is sexually mature or not, and there is a chronic form in which allergic tests are constantly positive; (2) in man the specific allergic condition can persist almost indefinitely; a chronic form does exist; the Coombs, and complement-fixation tests are advisable as well as agglutination.

W. K. Dunscombe

Ramah, S. J., Chomet, B., McLean, J. & Lemke, Catherine. **Pulmonary Granuloma due to Brucellosis.** *J. Amer. Med. Ass.* 1959, Aug. 1, v. 170, No. 14, 1665–7, 3 figs.

The authors report the finding of a granuloma, from which *Brucella suis* was cultured, in a resected segment of lung. Three similar cases were reported by Weed and Clagett [this *Bulletin*, 1956, v. 31, 1101]. The present case was complicated in that the patient, a man 42 years of age, first presented with an empyema of the left lower chest from which a haemolytic streptococcus was cultured. After rib resection and penicillin the condition improved but subsequent radiographs during the next year showed a persistent, well defined, round opacity in the lower part of the left lung. A wedge resection included a spherical firm nodule 2 × 1·8 × 1·5 cm. The nodule showed a large zone of caseous necrosis with hyalinization and focal calcification. At the periphery there were granulomatous changes with an occasional giant cell. Investigations other than for *Brucella* were negative. Although *Br. suis* was cultured from the granuloma the serum examined twice after operation showed no brucellar agglutinins. This has been found before in well encapsulated granulomatous lesions [Weed *et al.*, this *Bulletin*, 1952, v. 27, 655]. It is not known if the streptococcal infection preceded, accompanied or followed the brucellar infection.

Frederick J. Wright

Elberg, S. S. **Immunization against *Brucella* Infection. 7. Immunological and Epidemiological Studies in Córdoba, Spain.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1033–52. [25 refs.]

"The author describes a study, carried out in the Province of Córdoba, Spain, to test the efficacy of a live vaccine prepared from the Rev I strain of *Brucella melitensis* against caprine brucellosis and to determine

the extent of natural infection in goats and humans in the Province.

"It was found that the vaccine significantly increased the resistance of the goats to infection without inducing a carrier state of the vaccine strain and that the immunity persisted for at least 15 months—the period of test.

"Serum agglutination tests, milk ring tests, and milk culture tests on goats showed that approximately 16–29% of the individual animals examined would be considered infective on the basis of one or other of the tests. Of the 118 herds tested, 111 were discovered to be harbouring infected animals.

"Serum agglutination tests on humans revealed that 25 of the 880 people tested (2.8%) had titres of 160 International Units (IU) or above and that, on the basis of a diagnostic titre of 80 IU or above, 7% of the population would be regarded as showing evidence of a past or present infection."

SIL'CHENKO, V. S. **Epidemiological and Clinical Features of Tularaemia caused by Waterborne Infection.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 5/6, 788–95, 2 figs. [27 refs.] [Translated from Russian.]

The authors have found that the usual cause for water-borne tularaemia is the presence of dead infected water-rats. The duration of outbreaks depends more on the time elapsing before the source of infection has been traced and eliminated than on any other factor such as the climate, season or route of infection. Outbreaks are more frequent in autumn and winter when wild rodents migrate into inhabited places. When infection has resulted from washing in infected water, the disease is bubonic, ulcero-glandular or oculo-glandular in form, and after paddling the inguinal glands are found infected. When the infection is from drinking water, ulceration in the pharynx and cervical adenitis may result but abdominal pain indicates that the gastro-intestinal tract is also frequently affected.

When closed water supplies are freed from rodent carcases and the water disinfected with chlorine fresh cases from these sources cease.

Where exposure to infected artificial or natural open water is liable to take place vaccination offers the best method of protection. *Frederick J. Wright*

WYSOCKA, Felicja, ZWIERZ, J., JÓZEFOWICZ, L., BRYC, Z., DURLAKOWA, Irena, ŁAZUGA, K., KARMANSKA, Krystyna & DĄBROWSKI, T. Epidemiologia gorączki błotnej na Lubelszczyznie w r. 1954–1955. **[Swamp Fever Epidemic in the Lublin District in the Years 1954–1955]** *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1958, v. 13, 341–61, 5 figs. [18 refs.]

The English summary appended to the paper is as follows:—

"In 1955 a typical summer epidemic of swamp fever was observed in the Lublin district; it was more widespread than in the previous years and occurred in nearly all regions of the district. In the Tomaszów Lubelski region, where the investigations were conducted with special care, 552 cases were recorded. The epidemic had there a diffuse character, but its framework followed the configuration of waters and of marshland. Higher incidence was noted in those parts of the Tomaszów Lub. region where greater numbers of rodents were caught and where the configuration of the terrain and character of soils allowed surface waters to remain longer after the abundant July rainfall. The low sanitary and hygienic level of the Tomaszów Lub. region was an important epidemiological factor. Labour conditions in the country were the main source of infection; hay-makers were affected most frequently.

"In regions traversed by the line of works at the Wieprz—Krzna Canal there occurred cases of swamp fever. During examination of groups of workers some foci were found near the Canal. Only those workers were affected who, besides working at the Canal, pursued also their agricultural occupations. No evidence can be therefore given of their having contracted the disease during their work at the construction of the Canal.

"The course of the disease was gravest during the culmination of the epidemic. The same clinical type, in which organic symptoms, especially on the part of the liver, prevailed on the meningeal ones, was observed on the whole area of the epidemic. The disease was produced most often by *L. grippotyphosa*, and much less frequently by *L. sejroe*. There is serological evidence that in some persons the disease was produced by *L. saxkoebing* and *L. australis* B., which so far have not been found in the human material of the Lublin district.

"Short duration of antibodies was characteristic. No recurrences of swamp fever were observed, although this is theoretically possible because of the existence of several serotypes in the endemic foci, which was proved by examination of the rodents. However, observations aimed at detecting possible occurrences were very scanty and should be extended in the future."

CZARSKI, Z. & WAJDA, K. Objawy neurologiczne u chorych na gorączke błotną w epidemii na Lubelszczyznie w r. 1955. **[Neurological Symptoms in Patients suffering from Swamp Fever during the 1955 Epidemic in the Lublin District]** *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1958, v. 13, 389–93.

The English summary appended to the paper is as follows:—

"The authors' observations show that during the 1955 epidemic of swamp fever in the Lublin district the most frequently noted neurological symptom was meningeal irritation. This was often accompanied by discrete diffuse signs of an affection of the central nervous system and in a smaller degree, of the peripheral nervous system.

"Changes in the cerebro-spinal fluid, such as a slight increase of protein level, decrease of sugar level, and pleocytosis, were found in sporadic cases only."

ZWIERZ, J., DURLAKOWA, Irena, KARMANSKA, Krystyna, ZWIERZCHOWSKI, J., ŁAZUGA, K. & KORCZYNSKA, Alina. Badania fauny w ogniskach epidemii leptospiroz w powiecie Tomaszów Lubelski. [**Investigations of the Fauna in the Foci of Leptospirosis Epidemic in the Tomaszów Lubelski Region**] *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1958, v. 13, 421–37.

The English summary appended to the paper is as follows:—

"The scientific expedition stayed at Tomaszów Lubelski from 1st July to 1st November. The Department of Leptospirosis Research carried out bacteriological, serological and biological investigations. 1034 bacteriological tests were carried out in 468 persons and 68.8 per cent of positive results were obtained. Out of 322 serologically positive individuals, 220 (68.32 per cent) reacted with the serotype *L. grippotyphosa*, 55 (17 per cent) with *L. sejroe*, 13 (4 per cent) with *L. saxkoebing*, 6 persons with *L. australis B.*, and 2 with *L. pomona*. The titre oscillated between 1 : 100 and 1 : 409600. In the majority of patients antibodies appeared between the 4th and the 10th day.

"Bacteriological tests were carried out in feverish patients only. Out of 243 bacteriological tests performed in 225 persons, 112 positive cultures were obtained, from which 44 strains could be identified. 35 strains behaved like *L. grippotyphosa*, 8 like *L. sejroe*, and one will probably prove an independent serotype. In 69 biological tests 37 guinea pigs showed positive serological reactions. During the expeditions 919 rodents and other small animals belonging to 16 species were examined: 435 *Microtus arvalis*, of which 59 reacted serologically; 7 strains were cultured, of which one is probably a new serotype; 159 *Mus musculus*, of which 17 reacted positively; 6 strains were isolated and 2 proved to be *L. sejroe*; 75 *Arvicola terrestris*, of which 12 were serologically positive; 3 strains were isolated, among them 2 *L. sorex*; 61 *Fiber zibethicus*, serologically positive 28; one strain *L. sejroe* was cultured; 44 *Rattus norvegicus*, 2 serologically positive; one strain *L. sejroe* was obtained; 32 *Apodemus silvaticus*, 2 serologically positive; 2 strains were isolated, of which one *L. sejroe*; and the other *L. sorex*; 27 *Erinaceus roumanicus*, 5 serologically positive; 2 strains were isolated: *L. sorex* and *L. bataviae*; 25 *Sorex araneus*, 1 serologically positive; 2 strains of *L. sorex* were obtained; 23 *Neomys fodiens*, 3 serologically positive; no strain was cultured; 10 *Apodemus agrarius*, 1 reacted positively; 10 *Cricetus cricetus*, 2 serologically positive; 9 *Micromys minutus*, all serologically negative; one strain was isolated; 3 *Talpa europaea*—negative; 2 *Sorex minutus*, serologically negative; 1 strain of *L. sorex* was cultured; 2 *Crocidura leucodon*—negative; 2 *Mustella nivalis*—negative:

"The majority of the animals reacted serologically with *L. grippotyphosa*, and then with *L. sejroe*.

"The authors examined 1835 domestic animals and obtained positive results in 30·3 per cent. The animals reacted with the following serotypes: *L. grippotyphosa* 38·7 per cent, *L. icterohaemorrhagiae* 21 per cent, *L. sejroe* 17·4 per cent, *L. saxkoebing* 13·3 per cent, *L. canicola* 3·1 per cent, *L. pomona* 2·6 per cent, *L. autumnalis* 1·1 per cent, *L. australis A* 1·6 per cent, *L. australis B* 0·6 per cent, *L. mitis* 0·6 per cent.

"The authors have demonstrated that wild and domestic animals are carriers of different serotypes of Leptospira. In this connection it may be supposed that animals had a certain part in infecting the soil and water, which produced the epidemic."

AMMONS, J., GALTON, Mildred M., STARR, L. E., MENGES, R. W. & LEMAISTRE, C. **Human Leptospiral Infection due to one of the *Leptospira australis A* Group. Report of a Case in the United States.** *Southern Med. J.* 1959, Aug., v. 52, No. 8, 900–902, 2 figs.

"A patient with leptospirosis due to a member of the *Lept. australis A* serogroup has been reported. This is believed to be the first detected human infection with a member of this serogroup in North America."

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

GUPTA, R. N. & SHOME, S. K. **Dermatomycoses in Uttar Pradesh. An Analysis of 620 Cases.** *J. Indian Med. Ass.* 1959, July 16, v. 33, No. 2, 39–42.

An analysis of 620 cases of superficial mycotic infection reporting to the Mahatma Gandhi and Associated Hospitals, Lucknow, shows that 75% may be classified as tinea cruris and tinea corporis. The organisms responsible were *Trichophyton rubrum* (56·7%), *T. mentagrophytes* (31·7%), *Epidermophyton floccosum* (1·9%) and others (9·6%). *Peter Abbott*

RITCHIE, E. B. & PINKERTON, Mary E. ***Fusarium oxysporum* Infection of the Nail. Report of Cases.** *Arch. Dermat.* 1959, June, v. 79, No. 6, 705–8, 6 figs.

Two cases of thumb-nail infection by *Fusarium oxysporum* (WOLLENWEBER and REINKING, *Die Fusarien: ihre Beschreibung, Schädwirkung und Bekämpfung*, 1935, Berlin: Parey) are described with mycological notes. In the first, a black patch of discoloration was present on the under side of the nail plate. Cultures on Littman's ox-gall agar containing actidione and chloramphenicol

remained apparently sterile until the third week when the fusarium appeared as a uniform growth on the nail particles. The same species was isolated from a second collection of nail scrapings, but a third collection yielded on culture a fungus colony which, though bearing *Fusarium conidia*, was pink and glabrous ("reminiscent of Cephalosporium"). In the original culture non-septate ovate conidia (microconidia) were present as well as the septate sickle-shaped conidia. Sections of the nail plate revealed an interlaminar growth of the mycelium. In the second case, a greenish black discoloration was present in the distal third of the thumb nail. Microscopic examination revealed dense masses of spores. Culture yielded a species of *Candida* and *Pseudomonas pyocyanea* in addition to *Fusarium oxysporum*. In sections of this nail stained by the periodic-acid-Schiff technique compact masses of spores were present on the under side only. In sensitivity tests, aqueous merthiolate [thiomersal] (1:1000) was found to be the strongest inhibitor of this species among a selection of disinfectants and in therapeutic trials this preparation or the tincture was curative in 4 to 6 months in both patients.

C. J. La Touche

MITCHELL, A. D. & MITCHELL, D. M. **Griseofulvin in the Treatment of Favus.** *Irish J. Med. Sci.* 1959, Aug., 6th Ser., No. 404, 363–4.

An account of a patient treated with 2 gm. daily by mouth for some 3 months, followed by 1 gm. daily for 1 month. Clinical response was impressive and no side-effects appeared.

KNIGHT, R. A., CORAY, S. & MARCUS, S. *Histoplasma capsulatum* **and** *Blastomyces dermatitidis.* **Polysaccharide Skin Tests on Humans.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 264–6.

"Skin tests were carried out on 134 persons injected with histoplasmin, blastomycin and polysaccharides derived from broth in which the yeast phase of *H. capsulatum* and *B. dermatitidis* was grown. The histoplasmin and the *H. capsulatum* polysaccharide were equally sensitive. The *B. dermatitidis* polysaccharide yielded 5 positive reactions among persons exhibiting a concomitant histoplasmin sensitivity. The relative specificity of these reactions could not be determined."

HORTON, G. E., LARKIN, J. C. & PHILLIPS, S. **Acute Pulmonary Histoplasmosis.** *Southern Med. J.* 1959, Aug., v. 52, No. 8, 912–18, 5 figs. [20 refs.] Discussion 918–19.

"This case report illustrates acute pulmonary histoplasmosis, a disease which can be a problem in recognition, diagnosis and management. The discussion includes differential diagnosis, various diagnostic procedures and the management of this infectious disease."

LITTLE, J., BRUCE, J., ANDREWS, H., CRAWFORD, K. & MCKINLEY, G. **Treatment of Disseminated Infantile Histoplasmosis with Amphotericin B.** *Pediatrics.* Springfield, Ill. 1959, July, v. 24, No. 1, 1–6, 2 figs. [19 refs.]

4 babies, 3 of them under 9 months old, were treated for disseminated infantile histoplasmosis with daily intravenous injections of Amphotericin B. The dosage varied between 0·25 and 1·0 mgm./kgm. and was given over a 6-hour period dissolved in 5% dextrose solution in a concentration of less than 1·0 mgm. per 10 ml. Toxic effects were seen in 2 cases; one had daily febrile reactions and the other had chills, fever and an anaphylactoid reaction with peripheral cyanosis which, however, responded to antihistamine drugs and injections of adrenaline in oil.

In each case the treatment was continued for only 28 days or less and the response was gratifying: all were discharged free of symptoms and were apparently normal some months later.

Peter Abbott

FARIÑAS, P. El tratamiento de la moniliasis de los pliegues cutáneos con la preparación 45705-A (Polvo conteniendo Micostatín, Neomicina y Graneodín). (Informe sobre 13 casos tratados.) [**Treatment of Candidiasis of Skin Folds with Preparation 45705-A, a Powder containing Mycostatin, Neomycin and Graneodin**] *Bol. Soc. Cubana de Dermat. y Sifil.* 1958, Sept.–Dec., v. 15, Nos. 3/4, 140–43.

Each gramme of this powder contains Mycostatin (nystatin) 30 mgm., neomycin 2·5 mgm. and Graneodin [which itself contains neomycin and gramicidin] 0·25 mgm. The powder was applied locally 3 times each day, without other local medication. The author treated 13 patients with lesions in axillae, groins and other folds of skin, all confirmed by culture. The results were very good in those of recent origin, in which the lesions were moist and itching; these cleared usually within a few days. In one patient with diabetes the lesions were resistant. In 2 controls with mycotic lesions not due to *Candida* the response was poor.

Charles Wilcocks

VILLAR, T. G. Considerações sobre dois novos casos de "aspergiloma pulmonar". [**Observations on Two New Cases of Pulmonary Aspergilloma**] *Gaz. Méd. Portuguesa.* 1959, Mar.–Apr., v. 12, No. 2, 117–33, 21 figs. [47 refs.]

The English summary appended to the paper is as follows:—

"Two new cases of 'aspergilloma of the lung' are presented, both of which were recognised many years after being filed away under different diagnosis.

"The first was a ten year old boy with a tuberculous lymph-note cavity who had enormous hemoptysis. At operation a granular mass was spilled from the cavity into the bronchial tree, killing the child by bronchial obstruction.

"The second case was that of an adult woman, diagnosed as a lung abcess, but whose X ray picture was

somewhat strange. At operation a 'putty-like' mass was found in the cavity.

"On reviewing the pathological slides of the content of the cavities this was found to be made up of a mycelia with many 'dead' and some calcified aspergilli.

"In both cases, in retrospect, the X ray images were found to be pathognomonic of 'pulmonary aspergilloma.' Some curious aspects of the cases are pointed out, especially the fact of 'dead' aspergilli producing clinical symptoms while acting purely as a foreign body.

"As an addenda a case is presented which was diagnosed preoperatively based on the experience gathered from the study of the patients described above."

PIMENTEL, J. C. Novos aspectos morfológicos do "aspergiloma pulmonar". Seus prováveis estádios iniciais e residuais. [**New Morphological Aspects of Pulmonary Aspergilloma. Probable Initial and Residual Stages**] *Gaz. Méd. Portuguesa.* 1959, Mar.–Apr., v. 12, No. 2, 195–210, 23 figs.

The English summary appended to the paper is as follows:—

"The author describes a certain number of clinical pictures which he thinks he might interpret as initial and residual stages of the 'broncho-pulmonary aspergillomas.'

"The initial stages are morphologically marked by the presence of mycelium masses (which it has been possible to identify in one of the cases as 'Aspergillus Fumigatus'), the signs of which vary between corn grains and olives, inside broncho-pulmonary cavities, whose characteristics are similar to those of a 'constituted aspergilloma' (figs. 1, 2, 3). This initial stage does not show any clinical or radiological manifestation and has been identified in the course of a study of 205 parts resulting from exercises carried out for mere research.

"The aspects which the author interprets as residual stages may appear either in the form of a mycelium mass, necrosed and softened in the lumen—or also incorporated in the wall—of 'infected bronchiectases' or of chronic abcesses of the lung (figs. 4, 5, 6, 7, 9, 10, 11 and 12); or in the form of cavernolytes or broncholytes, formed by calcification of the fungus mass (figs. 13, 14, 15, 16, 17, 18, 19, 20 and 21). The fact that some aspects, very much suspected of corresponding to residual stages of the 'aspergillomas' (fig. 23) have been observed in bronchiectases of the lower lobes, leads to the assumption that the frequency of this localization may be less rare than is generally believed.

"The pictures observed are perfectly clear in presence of the findings verified in a study of 15 cases of 'broncho-pulmonary aspergilloma' (fig. 22)."

[See this *Bulletin,* 1959, v. 34, 226.]

See also p. 1262, RUYSSEN, **Commentary on a Case of Aspergillosis and Bronchiectasis occurring in a Coalminer suffering from Pneumoconiosis.**

Rheumatic Diseases

GLYNN, A. A., GLYNN, L. E. & HOLBOROW, E. J. **Secretion of Blood-Group Substances in Rheumatic Fever. A Genetic Requirement for Susceptibility?** *Brit. Med. J.* 1959, Aug. 29, 266–70. [18 refs.]

In a previous paper (GLYNN *et al. Lancet,* 1956, v. 2, 759) the authors reported that, of persons who had had rheumatic fever, an undue proportion were non-secretors in saliva of ABH blood group substance. They were, however, not satisfied with their data on the population frequency of non-secretors and with certain technical aspects of the work. The present paper gives estimates of Lewis and ABH secretor genotypes and phenotypes in the population based on the examination of 669 school children. ABH secretor estimates are based on the phenomenon of inhibition of the natural agglutinins of human 'O' cells by *Ulex* seed extract, and the Lewis estimates on the frequency of Le^a substance in saliva detected by using rabbit anti-Le^a precipitating serum. The two responses are mutually exclusive because Le^a substance, although detectable in the saliva of non-secretors, is not detectable in the saliva of secretors with the rabbit anti-serum precipitating technique. Le^a substance was detected in 21% of the children, H substance in 77% and neither in 2%.

From these data, assuming independent segregation of genes at Lewis and secretor loci, and Ceppelini's hypothesis about Lewis and secretor inheritance and interaction, estimates are made of the genotypes and saliva phenotypes in respect of Lewis and secretor and of the Lewis red cell phenotypes in the population. With these data as controls, comparison is then made of the results of saliva tests for both substances in persons who have had rheumatic fever with those of the control children.

The comparisons showed that 28·9% of rheumatic fever subjects and 22·9% of control children were non-secretors of H substance in saliva ($\chi^2 = 5{\cdot}9$ and $P<0{\cdot}02$). Of rheumatic fever subjects 27·5% and of control subjects 21·2% had Le^a substance in the saliva ($\chi^2 = 8{\cdot}8$, $P<0{\cdot}01$). These findings are impressive and enhance considerably the validity of the conclusions previously published.

In the discussion a hypothesis is advanced of the nature of the genotype (in respect of secretor status) concerned with susceptibility to rheumatic fever. It is postulated that a gene "*se*" recessive to its allele "*Se*" plays a part in determining susceptibility and that those at risk of rheumatic fever in a population are the homozygous (*se*/*se*) and heterozygous genotypes (*se*/*Se*). Put in another way, the susceptible subjects in a population would be the sum of the *se*/*se* and *se*/*Se* genotypes, although *se*/*Se* genotypes cannot be distinguished from

Se/Se genotypes serologically. However, an estimate is available from the data for the proportion of rheumatic fever subjects who are non-secretors, being 29·1% and on this hypothesis all these would be either *se/se* or *se/Se* so that the proportion who will be *se/se* would be $\frac{se/se}{se/se+se/Se}$. Substituting the estimated genotype frequencies from the control children, the estimated proportion of *se/se* genotypes, *i.e.* non-secretor phenotypes, in the population would be *31·4*%. With the numbers available this is not, as the authors point out, significantly different from the observed proportion of 29·1%, so that this finding is not incompatible with the genetic hypothesis for susceptibility advanced.

The authors, in appendices, attempt to see if such a hypothesis could be reconciled with the frequency of affection of the sibs and parents affected with rheumatic fever compared with that in the general population. As they clearly realized this, if an interesting, is a hazardous procedure. Age of onset and other complications suggest that study of the relatives of rheumatic fever subjects matched with controls would be the more valid comparison; particularly as estimates of the frequency of the condition in the population are scanty and must be rather inaccurate in view of diagnostic difficulties. In face of a falling incidence of rheumatic fever, or at least of recognizable manifestations, it is difficult to be happy about the procedure. In so far as data are available it would appear that the frequency in parents and in sibs of rheumatic fever subjects is increased considerably more relative to population frequency than this theory would suggest. To explain this they suggest that other factors, genetical and environmental, contribute to susceptibility.

[This is a most interesting and useful paper. It seems to establish quite firmly the greater susceptibility to rheumatic fever of non-secretor subjects. The genetic hypothesis must, however, as the authors remark, be considered with some reserve. Apart from uncertainties about the nature and inheritance of Lewis antigens and their relationship to secretor status, the hypothesis of the genetical mechanism advanced has no proved counterpart in human or experimental genetics. Although this is a negative argument reasons could be advanced which suggest that such a mechanism is unlikely.

In effect the allele "*se*" is postulated as dominant in determination of susceptibility but recessive in respect of its detectability in saliva. As from the data the relative frequencies of the genotypes in the population are approximately *se/se* : *se/Se* : *Se/Se* = 1 : 2 : 1, then approximately 75% of the population are on this hypothesis susceptible. Only less than one-tenth of that proportion of the population ever have the disease, however, so that the 'manifestation' rate must be postulated as very low. This always makes reconciliation with a simple genetical hypothesis well nigh impossible. A simple genetical hypothesis involving the secretor locus must assume that the *se/Se* genotype is at least more susceptible than the *Se/Se* but there can be no demonstration of that necessary condition until individuals with *se/Se* genotypes can be detected. It seems just as likely in the absence of the necessary evidence that rheumatic fever can occur in *Se/Se* individuals given other suitable and probably multifactorial contributions to the genotype and from the environment. This is, of course, not incompatible with a real increase in frequency of the disease in non-secretors.] *Alan C. Stevenson*

De Silva, S. **Incidence of Rheumatic Fever in Ceylon.** *Arch. Dis. in Childhood.* 1959, June, v. 34, No. 175, 247–9, 1 fig.

"Conflicting views have been expressed about the incidence of rheumatic fever in the tropics." In Ceylon investigations have led to the opinion that the general picture of rheumatic infection and rheumatic carditis does not differ in any important respects from that seen in non-tropical countries. This is probably quite true of rheumatic infection in the adult. In the present paper the author presents the results of his investigation of the incidence and manifestations of the disease in the children of Ceylon. Tables set out the statistics of incidence as seen in the admissions to the Lady Ridgeway Hospital for Children, Colombo (400 beds) in the individual years during 1953–57. The aggregate figures for the 5 year period were 70,292 admissions of which 560 (0·7%) were for rheumatic disease. The percentage of cases of carditis among these rheumatic infections was 35%. These figures of incidence are compared with those published for the Hospital for Sick Children, Great Ormond Street, London, for the periods 1919–20, 1946–50, 1949–56 and 1957, where although the incidence of rheumatic infection has lessened very greatly, the proportion of cases with cardiac manifestations has remained high at over 50%. Clinically rheumatic fever in childhood in Ceylon appears to run a mild course, cardiac complications are much less common than in temperate climates and cutaneous signs and chorea are very rarely seen. "The most common age of occurrence is in late childhood, from about 9 to 12 years." Among adults the figures of admissions to the General Hospital Colombo during 1952–57 were that among 3,538 cases of rheumatic disease in the total of 355,401 admissions there were 2,848 (80%) cases of carditis.

[The criteria adopted for the diagnosis of carditis are not stated.] *M. E. Delafield*

vorhanden? Search 17.

Cancer

DOLL, R. **Occupational Lung Cancer: a Review.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 181–90. [68 refs.]

Study of occupational factors was the method which led to the discovery of first pure carcinogen. There is hope that the further investigation of occupational causes will make an important contribution to knowledge of the fundamental mechanisms of carcinogenesis.

Already at least 5 independent industrial risks have been established: radioactivity, nickel, chromates, asbestos and gas production. Suspected risks are exposure to arsenic and iron and possible risks include isopropyl oil, beryllium and copper. There are theoretical reasons for thinking that the inhalation of petrol or diesel oil fumes, because these contain measurable quantities of 3:4 benzpyrene and other carcinogenic polycyclic hydrocarbons, might cause cancer of the lung but investigations so far have failed to support this [see, for example, this *Bulletin*, 1957, v. 32, 858]. Likewise there is no conclusive evidence that pneumoconiosis is aetiologically related to lung cancer [*ibid.*, 1955, v. 30, 766]. MORGAN [*ibid.*, 1959, v. 34, 242] suggested that the cases of cancer of the nose and accessory sinuses, which occurred among workers engaged in the production of nickel by the gaseous carbonyl process, might be due to arsenic which occurred as an impurity in the sulphuric acid used in the extracting processes. For various reasons Doll does not support this view. He does not, however, deny that inorganic arsenic in the air may produce lung cancer, provided the amount present is sufficient to produce gross evidence of arsenicism. In the absence of such evidence, he submits that it is most unlikely that the amount of arsenic inspired could be sufficient to account for any important industrial risk of lung cancer.

Although cancer of the lung is now a common cause of death in the general population—10% of all deaths among men from 45 to 64 years—its prevalence is so low that, even in the presence of a major risk, the examination of as many as 1,000 workers may fail to reveal any cases on a single occasion. There is often a long latent period before the disease becomes manifest. The need is for planned prospective studies.

[Within the limits of its prescribed length this is an excellent, well documented critical review of current knowledge of the subject. It should be read in conjunction with the chapter on occupational cancer in the latest Annual Report of H.M. Chief Inspector of Factories for the year 1958 [this *Bulletin*, 1960, v. 35, Jan.]. At the International Conference on Pneumoconiosis held at Johannesburg in February, 1959 (Proceedings in press, J. & A. Churchill, London), Dr. J. C. WAGNER recorded his unique experience of mesothelioma of the pleura complicating asbestosis in the Union of South Africa. In the course of recent very extensive mass radiography campaigns hundreds of cases of unsuspected cancer of the lung were discovered. A more thorough investigation of the employment history of these patients by experts might help direct attention to possible lines of further study at a time when industry is almost daily introducing new materials and processes.]

A. Meiklejohn

See also p. 1267, SUNDERMAN *et al.*, **Nickel Poisoning. IX. Carcinogenesis in Rats exposed to Nickel Carbonyl.**

HUEPER, W. C. **Carcinogenic Studies on Water-Soluble and Insoluble Macromolecules.** *Arch. Pathology.* 1959, June, v. 67, No. 6, 589–617, 28 figs. [52 refs.]

Numerous experiments have established that many synthetic and semi-synthetic water-insoluble hydrocarbon and silicon polymers can produce sarcomas at the site of implantation in rats and mice. More recently, it has been shown that some water soluble polymers may also produce reticulum cell sarcomas of the liver and peritoneal lymph nodes. These tumours, distant from the site of injection, arise in tissues in which the macromolecular material is aggregated and stored. Conflicting opinions have been expressed about the method by which the cancers are induced. Some investigators consider that specific chemical or physio-chemical properties of the substances are responsible: others consider that the effect is due to the physical status of the molecules and their ability to elicit the formation of a fibrous capsule which, as a result of prolonged non-specific irritation, leads eventually to the development of sarcoma. With this latter concept, the carcinogenic effect of the polymers might be analogous to that observed with the implantation of discs of certain metals.

In the present series of experiments, tests were conducted with 6 water-insoluble polymers and 24 water-soluble polymers (including 10 polyvinylpyrrolidones with average molecular weights varying from 10,000 to 300,000 and 11 dextrans with molecular weights varying from 37,000 to several million and differing in respect of their molecular shape). The results showed that cancers could be produced with 5 of the polyvinylpyrrolidones, 1 dextran, polyvinyl alcohol and silastic rubber and could probably be produced with some of the other substances but not with all. With the water-soluble polymers sarcomas developed in the reticulo-endothelial system. A few carcinomas in other organs, particularly the skin and uterus, may also have been due to the action of the polymers—either directly or indirectly. From these experiments it is not possible to recognize any particular chemical or physical properties of the substances which could have been responsible for the effect. It is, however, notable that silicon rubber having a net-like molecule with many cross-linkages had a strong carcinogenic effect, whereas a silicon latex with a linear molecule was, at most, weakly carcinogenic. In the author's opinion the total available evidence suggests that the toxic, pharmacological and carcinogenic effects of the synthetic and semi-synthetic polymers are mainly related to their chemical properties.

In the light of the experimental evidence caution is

required in the use of these substances for medicinal and cosmetic purposes. *Richard Doll*

MAHRBURG, S. Badania anatomiczno-patologiczne nad zmianami w tkance płucnej myszy po wydchaniu dymu tytoniowego. [**Anatomopathological Investigations on Changes in the Lung Tissue of Mice after Inhalation of Tobacco Smoke**] *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1958, v. 13, 35–46, 5 figs.

The English summary appended to the paper is as follows:—

"The author carried out experimental investigations on the influence of the smoke from the commonly used cigarettes on the lung tissue of mice. The mice were fumigated in an air-tight glass bell four times a day, 20 to 25 minutes each time. 10 animals were subjected to fumigation for 100 days, 40 animals for 150 days.

"On the strength of the obtained results the author found that 1. tobacco smoke when inhaled for a short period of time can produce in the parenchymal tissue of the lung an inflammatory reaction, often of a transient character. 2. After the first weeks there is observed a deposition of a great quantity of blood-derived pigment in parenchymal tissue and epithelium of the air-cells. 3. There arises the question of the influence of substances contained in tobacco smoke on the circulatory system of the lung tissue. 4. There is a marked difference in the histological picture beween short and long periods of smoke inhalation. Longer periods are characterized by (a) absence of inflammatory reaction, (b) occurrence of small extravasations in the lung parenchyma, (c) transformation of the cells of the epithelium of air-cells, their germination, and tendency to penetrate into the lumen of air-cells."

Dental Hygiene

MELLANBY, May, MARTIN, W. J. & BARNES, D., with the assistance of Gwenneth NEAL. **Teeth of 5-Year-Old London Schoolchildren (1957) with a Comparison of the Results obtained from 1929 to 1957.** *Brit. Med. J.* 1958, Dec. 13, 1441–3.

Except for 1953, reports on the teeth of 5-year-old London Schoolchildren have been provided by LADY MELLANBY and her co-workers at intervals of 2 years from 1929 onwards. This report gives the results of the 1957 survey, and enables one readily to see how the figures for 1957 compare with those for 1955 and earlier years.

The average hypoplasia figure for 1955 was 0·94 and the figure for 1957 was 0·74, so there was a substantial improvement in the structure of the dental enamel during that 2-year period. Nevertheless, the average caries figure for 1957 showed little change from that for 1955—the actual figures being 0·68 in 1955 and 0·66 in 1957. *Robert Weaver*

DE MEIRA, M. T. V. & DE SOUSA, H. T. Fluorose dentária em Cabo Verde. Estudo dum núcleo endémico na Ilha de S. Vicente. [**Dental Fluorosis in Cape Verde. Study of an Endemic Focus in St. Vincent**] *Anais Inst. Med. Trop.* Lisbon. 1957, Sept.–Dec., v. 14, Nos. 3/4, 429–54, 14 figs. on 7 pls. & 1 map. [12 refs.] English summary.

In one small village where the drinking water contains 3·3 to 4·55 parts per million of fluorine, 73% of the inhabitants showed dental fluorosis. Other villages had less fluorine in the water and less fluorosis. The incidence of dental caries was high in the village with a high incidence of fluorosis. There is evidently an optimal concentration of fluorine (0·5 to 1·0 p.p.m.) to confer protection against caries. *Charles Wilcocks*

Mental Hygiene

LAMBO, T. A. **A Form of Social Psychiatry in Africa (with special reference to General Features of Psychotherapy with Africans).** *Bureau Permanent Interafricain de la Tsé-Tsé et de la Trypanosomiase No. 2/0* [Léopoldville (Congo Belge)]. 14 mimeographed pp. 1959, July.

The author, an African psychiatrist in Nigeria, gives further information as to the results achieved by out-patient treatment since his previous report [this *Bulletin*, 1957, v. 32, 451]. Out-patients are accommodated in villages near to the hospital by willing landlords, a proportion of whom are employees of the hospital. The villages provide a suitable rural environment for rehabilitation. The patients usually have accompanying relatives as aids in this work carried out largely unconsciously by the village community but supervised by visiting medical personnel. The village communities are more tolerant than those of more highly developed communities, so that schizophrenics practising such asocial behaviour as indecent exposure do not cause trouble. As an extension of this work village farms have now been organized where chronic patients maintained on reserpine or chlorpromazine can be gainfully employed.

The author fully appreciates that the social upbringing of many Africans is changing rapidly but few have shed

all reliance on traditional beliefs and customs. The African tends to accept visitations by ancestors in dreams as realities and the author quotes the case of one sophisticated African, suffering from a severe anxiety state, who quickly recovered after sacrificing a goat as instructed in a dream so he believed, by his deceased grandfather. Attempts are being made to rehabilitate in posts in industry the educated Africans who do not recover quickly. *Frederick J. Wright*

BAKER, A. P. **Mental Health in Nyasaland.** *Bureau Permanent Interafricain de la Tsé-Tsé et de la Trypanosomiase No. 3/0* [Léopoldville (Congo Belge)]. 5 mimeographed pp.

The only mental hospital in Nyasaland is at Zomba. The author gives statistics relating to patients in it but he also considers the general problem of mental disease in Nyasaland. Experience at Zomba has shown that, provided a psychiatrist can anticipate aberrant behaviour, physical restraints and specially built wards are unnecessary and the resulting economy permits of expansion of trained staffs. As noted in Nigeria [LAMBO, see above], the African peasant is tolerant of abnormal behaviour which is not unduly agressive. Admissions to Zomba, therefore, occur progressively less frequently from areas at increasing distances. The author, through the Director of Medical Services, has instituted chlorpromazine treatment by district medical officers for patients with acute psychoses and relapsing schizophrenia. These measures prevent the central specialized hospital from becoming over-crowded and it is hoped prevent abnormal states from becoming firmly established. Case recording is being developed on a descriptive rather than a diagnostic basis and it is hoped from a study of this material to devise some simple diagnostic and therapeutic principles which district medical officers will be able to apply successfully locally.

[The principle of local rehabilitation agrees with the policy advocated in Nigeria by Lambo (*loc. cit.*).]

Frederick J. Wright

ROSEN, G. **Social Stress and Mental Disease from the Eighteenth Century to the Present: Some Origins of Social Psychiatry.** *Milbank Memorial Fund Quarterly.* 1959, Jan., v. 37, No. 1, 5–32. [67 refs.]

There is today a widespread belief that mental health is inextricably bound up with the social environment in which people live. Society could, but has not, achieved those conditions essential for the mental health of its members. The view is currently held that this fact is itself a challenge to society to examine the causes of its own sickness. Social change rather than the complexity of society may be the most significant factor for examination. Through the 18th and 19th centuries the way in which currently held opinions have developed is traced.

RUSH in 1774 and again in 1799 quoted the experiences of the American War of Independence to show the relation between mental health, political conviction and social upheaval. Throughout the 19th century there was a steady flow of discussion on the kindred questions "Is mental illness on the increase?" and "What are the causes of mental illness?". From decade to decade a wide variety of views was expressed. BURROWS took the view that social factors, including "social upheavals" were potent forces in mental health. At the same time he disputed the earlier held view that "the savage", untarnished by civilization, was free from mental disorders. BROWNE deplored the absence of reliable evidence but presented figures indicating a relationship between increased mental illness and an increase in the wealth of the community. He also examined the incidence of insanity by social class and by occupation. But on all sides it became more clear that the data necessary for a valid judgment were not available. No figures existed either for the current or for any previous population of the mentally ill.

JARVIS therefore turned his attention to the *causes* of mental illness in order to see if "causes" were on the increase. He concluded that insanity was related to the increasing complexity of civilized life and therefore likely to be itself on the increase. Similar views were held by many authorities in many countries. By the mid-19th century the belief was widespread that there was an ever increasing population of the insane, and that it was largely due to the increasing complexity of life though there were numerous variations to this theme.

In 1857 HAWKES proposed that a preventive programme for community mental health should be instituted. The principles governing the application of a public health policy were, he argued, equally appropriate to mental health, and he made a powerful plea for a comprehensive social policy of preventive mental health. By this time the problem of mental disease, in terms of incidence, prevalence, trend, causation, prevention and community action, had been broached, and a foundation for the future had been laid.

ANDREWS, at the end of the century, was able to quote precise (though perhaps not accurate) figures of the incidence of insanity among different sections of the American and other populations. Andrews's discussion contained in essence the elements of the ecological study of mental disorder which are today well accepted procedures.

By the beginning of the 20th century studies of the differential incidence of mental disorders—including suicide—were numerous, and each study implied the need for further study. Thus from the 18th century to the present day the broad concept has existed that social stress is in some way related to the causation of mental illness. Within this framework various views have been put forward, and many have been rejected. Many of the views have lacked any supporting evidence, but gradually more facts have been accumulated.

More recently it has been possible to distinguish and define other variables that are relevant to the overall problems. Future research requires that the problems should be tackled from a wide variety of angles, and the historical approach should not be neglected.

H. G. Maule

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

SCOTT, T. S. **Moral Responsibility and Dangerous Chemicals. The Wyers Memorial Lecture, 1958.** *Trans. Ass. Indust. Med. Officers.* 1959, July, v. 9, No. 2, 57–65.

This lecture discusses the ethical position of doctors and employers in industry with regard to the manufacture and use of substances actually or potentially dangerous to health with special reference to the chemical industry. Both have a moral responsibility, the doctor in the recognition of the clinical manifestations of industrial disease and their association with exposure to toxic substances, the employer in the search for less toxic alternatives and the application of safeguards and close supervision.

Occupational cancer of the bladder is cited as a special example of the cooperation between doctors, employers, chemists and engineers in achieving the abandonment of the most potent carcinogen, beta-naphthylamine, and its replacement by the less toxic benzidine and alpha-naphthylamine. Safer alternatives have also been found for other substances whose complete prohibition is economically not feasible. Benzene, for example, as a solvent, can be replaced to a large extent by less toxic compounds, but in the chemical industry it is a basic raw material and is still widely used, but in conditions made safe by the application of modern engineering methods.

Animal experiments cannot be applied to every new chemical substance before it is used commercially but 2 cases are quoted in which they proved successful in preventing the manufacture in this country of compounds of high potential carcinogenicity—the insecticide 2-acetylaminofluorine, and the rubber chemical xenylamine.

The code of working practice drawn up by the Association of British Chemical Manufacturers in 1953 for the chemical industry recommended not only the selection of workers, general health supervision and the following up of those known to have been exposed to carcinogens and other long-term hazards, but also certain measures regarding plant hygiene methods of manufacture and handling of certain toxic substances and the chemical and engineering precautions necessary to prevent their ill-effects.

The heaviest responsibilities of the industrial doctor are to advise on the degree of danger to be expected from the manufacture and use of highly toxic substances, and on the extent of the precautions necessary to satisfy the required standards of safe working; to co-operate with employers, scientists and technologists in their efforts to attain these standards; and to watch for the first signs of any ill-effects on the health of the workpeople from the use of new compounds or of those already known to have caused such ill-effects.

Ethel Browning

GRANT, J. S. **The Development of Occupational Medicine.** *J. Roy. Inst. Pub. Health & Hyg.* 1959, Feb., v. 22, No. 2, 47–57, 4 figs.

COLLINS, C. P. **Accidents in a Naval Dockyard.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 208–15, 2 figs. [15 refs.]

"The high incidence of accidents in H.M. Dockyard, Singapore, during 1954 led to a more detailed recording and analysis in 1955–56". About 10,000 persons are employed in the dockyard. Of these, 7,122 males, an average figure over the years 1955–56, were principally concerned with industrial work and thus exposed more or less to the hazard of accidents. This number was made up of 2,298 Chinese, 3,680 Indians, 1,133 Malays and 11 Eurasians. About 250 women were also employed but no accidents among these were reported.

At the beginning of 1955 accidents were more accurately recorded by race, age, department, cause of accident and classified by severity in 3 categories. Each month a nominal roll of accidents was sent to the heads of the respective departments in order to pinpoint areas where most accidents were occurring and to enable them to take the necessary steps to reduce the accident hazard.

This action was followed by a remarkable drop in the number of accidents. There is a good general description of the accident experience in 1955 and 1956 with a number of tables which set out the annual and quarterly figures in male industrial workers classified by ethnic groups, accident rates per 1,000 workers by 11 categories of causation, number of work shifts lost, number of accidents by age and other particulars. There is also a comparison of some of the accident experience with that reported by H.M. Chief Inspector for the United Kingdom in 1955.

Some of the conclusions were:—

"The number of accidents reported were 1,794 (1955) and 805 (1956). Expressed as accidents per 100 employee-months this is 1·00 for Chinese, 1·01 for Indians, and 0·67 for Malays.

"The rates per 1,000 workers for 1956 for accidents requiring notification under the Factories Act, 1937, is shown as 9·1: the international accident frequency rate is 1·7."

Accident rates were highest for Chinese and Indians in the 26–35 year age group, and lowest at 56 years and over.

Most accidents occurred on Mondays with a slight secondary peak on Fridays

M. E. Delafield

GORDON, C., EMERSON, A. R. & PUGH, D. S. **Patterns of Sickness Absence in a Railway Population.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 230–43, 6 figs.

This is a detailed account of an investigation undertaken to collect morbidity statistics for a large industrial group which consisted of 14,074 men employed on the railways in Scotland. This number is 24% of the total railway male employees in Scotland. Sickness absence information as well as the nature of and reasons for changes of jobs were obtained for the 12 months from April 1, 1955. In this period the man-days lost in the year were 116,742 out of the total available man-days of 4,025,164—a proportion of time lost of 2·90%. From an analysis of the figures 6 indices of sickness absence were obtained and are defined under the titles of: (1) sick person rate, (2) episode rate, (3) average duration per person, (4) average duration per sick person, (5) average duration per episode and (6) average number of episodes per sick person. These various indices were used at suitable times in the extensive statistical analysis which is fully described and discussed. Tables and figures set out the results in detail. Particulars are given of the representative railway grades—manual, sedentary and administrative and supervisory—of the "railway research population" which was investigated. Aspects of the statistical analysis which were considered included: sickness indices by age, incidence of types of episode by age, comparisons with other industrial populations, daily variations starting days of sickness in the different grades, relation of sickness absence patterns to certain characteristics of grades and job changes due to sickness.

M. E. Delafield

JANSEN, G. Zur Entstehung vegetativer Funktionsstörungen durch Lärmeinwirkung. [**Effects of Noise on Physical Function**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 238–61, 5 figs. [15 refs.]

Much interest has of recent years been focussed on the effects of noise on health and a considerable number of scientific papers on these effects have been published [this *Bulletin*, 1959, v. 34, 133, 341, 447, 1010]. In addition to the well-known effect of noise on the auditory apparatus observers have described other physical effects which are distinct from the psychic disturbances from which some of those exposed to noise are known to suffer. The physical reactions evinced by some persons during exposure have been regarded as of purely temporary character since they tend to pass off in an hour or so after the noise has ceased, nevertheless the question remains whether frequent exposure to severe noise may bring about permanent pathological changes.

In the investigation which is fully described in this paper 1,005 workers were carefully interviewed and clinically examined. Particulars of these employees at 15 works are given in a table—the numbers engaged at 34 different types of work and the intensity of the noise to which they were exposed. The findings of the investigation are described with the help of tables and figures which give details of the many symptoms of which complaint was made and of the conditions found which were regarded as being definite disturbances of physical function. A statistical comparison was made of the frequencies of these possible effects of noise among 669 workers exposed to severe noise and the remaining 336 workers who worked under quiet conditions. The 669 workers exposed to noise had more symptoms and signs than the remainder. The signs which gave evidence of disturbance of function were mainly impairment of the circulation in the extremities, pallor of the skin and cardiac abnormalities—disturbance of rhythm, tachycardia and extra systoles.

M. E. Delafield

See also p. 1254, DOLL, **Occupational Lung Cancer: a Review.**

RUSKI, N. Štetno dejstvo capsaicina na čovečji organizam pri radu sa crvenom paprikom. [**The Harmful Effect of Capsicin on the Human Organism while working with Red Pepper**] *Higijena.* Belgrade. 1958, v. 10, No. 4, 304–9, 4 figs.

A clinical and laboratory investigation has been carried out on 110 persons working in a factory processing red peppers (*Capsicum crassum*) in Yugoslavia. A patch test with red pepper extract was positive in 13 of 14 workers who suffered from chronic occupational illness, and in 2 of 12 of a control group who were symptom-free. Atrophic tonsillitis was observed in 25% of workers, acute hypertrophic tonsillitis in 14%, essential hypertension in 17%, rhinitis in 12%, chronic conjunctivitis in 7%, and erosion of the nasal septum in 8% and perforation in 2%. The sedimentation rate was raised in 18 of 20 persons who had been working with red peppers for 3–13 years.

D. J. Bauer

JOHNSON, W. S. **An Investigation into the True Exposure of Arc Welders by means of Simultaneous Sampling Procedures.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 194–6, 1 fig.

This is a preliminary study of the concentrations of welding fume immediately outside of a welder's hood in the area normally sampled for measuring a welder's exposure and within the hood in the air actually breathed by the welder. For the purpose of the study a conventional welder's hood was fitted with a 1-inch diameter aluminium filter holder, which placed the filter immediately in front of the nose and mouth of the wearer of the hood. The filter medium used was glass fibre filter web cut into 1-inch diameter circles. To this a midget impinger pump was connected and sampling was done at the rate of 5 to 6 litres per minute. Samples were collected during a period of 4 months (July–October) in 2 welding shops where steel castings and weldments in sizes ranging from $\frac{1}{8}$ ton to 10 tons were repaired and fabricated. Simultaneous sampling of fume was done by means of the above filter and an electrostatic precipitator. The precipitator was held about 4 inches forward of the welder's ear and within 1 inch of the welding helmet at the same level as the filter holder. Tests were made

of the inherent sampling efficiency of the filter, compared with the precipitator, and the results show that the ratio of precipitator concentrations to filter concentrations ranged from 1·08 to 1·10. All the fume samples in this study were analysed for iron oxide by a modification of the o-phenanthroline method of PEPI (*Anal. Chem.*, 1950, v. 22, 560).

The results of the prolonged study are given in a table and on an average the concentration of fume collected by the electrostatic precipitator was about 3·5 times greater than that collected by the filter.

P. J. R. Challen

EVANS, R. B. **Aerosol Filtration with Fibrous Media.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 327–31, 6 figs.

A general account of the problems involved in air filtration.

MOSINGER, M., FIORENTINI, H., GRAS, A., GARCIN, C., EL FEKI, M. & CARTOUZOU, G. Intérêt d'une méthode pour l'étude expérimentale des pneumoconioses: introduction intrabronchique de la poussière après intubation trachéale à l'aide d'un bronchoscope chez le chien. [**A Method for the Study of Pneumoconiosis in the Laboratory: Intrabronchial Injection of Dust in Dogs by use of a Bronchoscope**] *C.R. Soc. Biol.* 1959, v. 153, No. 4, 646–7.

There are many routes, intraperitoneal, intratracheal, subcutaneous and conjunctival, whereby silicosis can be produced experimentally in laboratory animals. The use of small animals restricts the extent of investigations such as radiographic examination, measurement of silica in the blood and urine and tests of pulmonary function. These require the use of larger animals and the authors devised the following method of "dusting" dogs.

The animal is anaesthetized by the intravenous injection of sodium pentothal or nembutal. It is important that the anaesthesia should be deep enough to abolish completely the cough reflex. An ordinary bronchoscope is then introduced into the trachea as far as the bifurcation. This enables the investigator to direct the dust into the right or left lung or both. A rubber or plastic tube about 5 mm. in diameter is inserted into the bronchoscope and through this the appropriate dose of the dust suspension is injected by means of a 50 ml. syringe. The animal rarely suffers any immediate symptoms apart from dyspnoea, which disappears within 24 hours. By this method it has been found possible to produce simple and massive fibrosis.

A. Meiklejohn

MOSINGER, M. & CARTOUZOU, G. Sur la constitution histologique et cytologique du granulome silicotique péritonéal. Histiocytes argyrophiles. [**Histology and Cytology of Silicotic Granulomata in the Peritoneum. Argentophil Histiocytes**] *C.R. Soc. Biol.* 1959, v. 153, No. 4, 647–50.

In previous experiments the authors observed that by injection of large doses (4 gm./kgm.) of silica intraperitoneally in guineapigs it was possible to produce abnormally large silicotic granulomata. Alongside these tiny silicotic nodules developed. They compared the histological and cytological features of these lesions at the end of 2 months. The silicotic granulomata were composed of masses of reticulo-histiocytes and as in silicotic islets the cells were of 2 types: reticular cells which were non-argentophil and histiocytes which were strongly argentophil. The basic substance first formed in both types of lesion was PAS [periodic acid Schiff]—positive and metachromatic. In the large granulomata the ground structure was a diffuse reticulinosis with few collagen fibres whereas the small silicotic nodules of the same age were made up of numerous collagenous fibres and fibroblasts. Plasmocytes and mastocytes were less prominent in the giant than in the minute lesions.

A. Meiklejohn

MOSINGER, M., LISSITZKY, S., CARTOUZOU, G., SOUCHON, C., REYNAUD, J. & MIRANDA, F. Sur la composition en protéines du granulome silicotique expérimental du Cobaye. [**Nature of the Proteins in Silicotic Nodules Produced Experimentally in Guineapigs**] *C.R. Soc. Biol.* 1959, v. 153, No. 4, 650–54. [12 refs.]

To obtain silicotic tissue in amounts sufficient for chemical analyses 40 guineapigs were injected intraperitoneally with large doses of quartz suspended in saline. The animals were killed at the end of 2 months and the silicotic tissue removed and prepared for chemical investigation. The main object was to estimate the amount of collagen and associated proteins. For the purposes of the study collagen is defined as:

> "collagen means those proteins which are converted to gelatin by water at 100°C. or are soluble in 5% trichloracetic acid at various temperatures." [Abstracter's translation.]

The methods of chemical analysis for the various constituents are cited in the text and the results are tabulated.

It emerges that silicotic nodules in guineapigs contain very little collagen (3–5% of total proteins) after 2 months. Extraction of collagen by trichloracetic acid is highest at 100°C. and is almost double the figure for water.

A. Meiklejohn

DAUTREBANDE, L., BECKMANN, H. & WALKENHORST, W. **Studies on Deposition of Submicronic Dust Particles in the Respiratory Tract.** *Arch. Indust. Health.* Chicago. 1959, Apr., v. 19, No. 4, 383–91, 7 figs. [16 refs.]

Aerosols of indian ink, aluminium, calcium carbonate and iron oxide, in particles smaller than 2 microns diameter, were inhaled by subjects breathing through the nose at selected frequencies and tidal volumes. Samples of the original aerosol and of the exhaled clouds were taken with thermal precipitators, the latter being sampled:

(a) from the mixed tidal expired air (global expired air);
(b) from the end of the tidal air; and
(c) from the last portion of the alveolar air.

The samples were collected on formvar screens, shadowed with tungsten and photographed in an electron microscope. Enlarged photomicrographs were counted and sized. Depositions in the respiratory tract were computed by comparing counts from (a), (b) and (c) with those on the inhaled cloud.

At a respiratory frequency of 3 cycles per minute the total deposition in the tract was 55–65% (a), 80–85% (b) and 88–98% (c). These depositions fell at 32 cycles/minute to 23–31% (a) and 32–38% (b) but rose very slightly in the case of (c). The tidal volume fell from 2,000 cc. to 350 cc. when the frequency rose from 3 to 32 respirations/minute.

Size distribution data for the individual dusts were rather scattered but by counting them all together (without correcting for density which ranged from 1 to 5·6) minimum deposition was indicated around 0·25 micron for (a) and (b). The maximum particle size in (c) was about 1 micron and the deposition fell from 100% at 2 microns to about 83% at 0·03 micron.

The results were independent of concentration which ranged from 15,000 to 400,000 particles/cc.

[For an earlier study by the author, see this *Bulletin*, 1958, v. 33, 669.] *C. N. Davies*

Drasche, H. L'action biologique des poussières industrielles mixtes. [**Biological Effects of Industrial Mixed Dusts**] *Arch. Malad. Professionnelles.* Paris. 1959, July–Aug., v. 20, No. 4, 362–6.

At a group of large steel works in the Sarre region of France the workmen in some departments are exposed to very dusty conditions. The dust is a mixed dust composed mainly of oxides of iron but with only a trace of silica. An investigation was made into the effects of the dust on the health of workmen.

In a group of 140 workmen, who had been exposed to the risk for a minimum of 10 years, radiographic changes were observed in the lungs and these increased directly with the period of employment. The earliest changes were an increase in normal lung markings with superimposed micronodulation similar to that in coal-workers' pneumoconiosis.

410 men were investigated clinically and the results compared with those of a previous study of 1,389 men on the plant, who were not exposed to dust. It emerged that affections of the upper respiratory tract and maxillary sinuses—particularly the latter—were significantly more frequent among the steel workers than in the control group.

[Nowadays it is remarkable to find no analysis of smoking habits in such a study.] *A. Meiklejohn*

Perry, K. M. A. **Lung Disease due to Inhaled Dust.** *Postgraduate Med. J.* 1959, Aug., v. 35, No. 406, 470–75.

LaBelle, C. W. & Brieger, H. **Synergistic Effects of Aerosols. II. Effects on Rate of Clearance from the Lung.** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 100–105, 2 figs. [18 refs.]

"1. The rates at which inhaled foreign particulates are eliminated from the lung after exposure differ widely, the extreme values for the half-life in the lung being one hour for metallic iron particles and five and one-quarter months for beryllium sulfate. A part but not all of this variation is associated with differences in particle size, large particles, in general, being expelled more rapidly than small particles.

"2. Particulates reaching the lung in very small amounts may be retained in the lung for unexpectedly long periods. This would likely be true of the particulates present in the general atmosphere as a result of smog or fall-out. Predictions as to the effect of smog or fall-out which are based on analogies with industrial experience may be misleading, since industrial dust levels are commonly adequate to stimulate elimination by phagocyte production.

"3. The simultaneous administration of inert dust can accelerate the expulsion of biologically active particles from the lung when the latter are present in very small amounts. The greater lung burden increases the release of phagocytes.

"4. Accidental exposures to highly noxious particulates (e.g., radium sulfate aerosol) have occurred in the past and doubtless will occur in the future. More or less effective decontamination procedures have been developed both for internal and for external depots with the exception of the lung itself, where the hazard of such deposition is perhaps the greatest. It is at least conceivable that the synergistic stimulation of phagocytes by inert particles might permit therapeutic decontamination of the lung."

Beckmann, H. & Hilgers, A. Über Untersuchungen bei der Frühsilikose. [**Studies on Early Silicosis**] *Beiträge z. Silikose-Forschung.* 1959, No. 59, 1–37, 7 figs. [38 refs.]

The authors describe their findings in 118 coal face workers aged 23–42 years in whom silicosis appeared after a short period in mining. Haemoglobin, total red and white cell and differential counts, blood sedimentation rate, Takata reaction and coagulation band of Weltmann were normal. The total serum protein was slightly reduced (mean 6·5 gm.%) and paper electrophoresis showed a reduction of the serum albumin (54·6% of the total) and an increase in gamma globulin (18·9%), changes which are considered to indicate increased reticulo-endothelial activity. In 37 of the miners the urinary excretion of 17 ketosteroids was reduced and this is attributed to reduced adrenocortical function in early silicosis. In 7 additional cases active tuberculosis was found to promote the rate of development and extension of silicosis.

I. T. T. Higgins

Worth, G., Lühning, W., Muysers, K., Siehoff, F. & Werner, K. Das Residualvolumen bei schwerer Silikose mit perinodösem Emphysem. [**The Residual Volume in Massive Silicosis associated with Perinodular Emphysema**] *Beiträge z. Silikose-Forschung.* 1959, No. 59, 39–57, 8 figs. [17 refs.]

102 miners with silicosis stage III and unequivocal radiological evidence of localized emphysema near the mass were studied. 49 presented the characteristic clinical signs of emphysema; in 71 the residual volume determined by the hydrogen dilution method, was 35% or more of the total lung capacity; while in one-third

of all cases of advanced silicosis with localized emphysema the residual volume was normal. The authors suggest that bronchostenosis and resultant air trapping could lead to an under-estimate of the residual volume and so explain the normal values in some of these cases.

I. T. T. Higgins

SADOUL, P. & METZ, J. Les modifications circulatoires pulmonaires au cours des pneumoconioses. [**Changes in the Pulmonary Circulation in Pneumoconiosis**] *Arch. Malad. Professionnelles.* Paris. 1959, July–Aug., v. 20, No. 4, 443–5.

The assessment of disablement for compensation purposes in pneumoconiosis is difficult. Symptomatology, radiology, tests of ventilatory capacity and gaseous exchange in the lungs, separately and in combination, only assist partially. All too often impairment of pulmonary function is attributed too readily to emphysema. Disturbances of pulmonary circulation are not infrequent as shown by observations at necropsy and in life by angiography and cardiac catheterization. The incidence of such changes is sufficiently proved to justify the application of these procedures by experts preferably at clinics suitably equipped for the purpose. It is not always necessary, nor is it recommended, that these investigations should be used as routine practice, although in expert hands there is little risk involved. Though physicians concerned with pneumoconiosis cannot all undertake this specialized work, they should be familiar with the techniques and interpretation of the results. *A. Meiklejohn*

GUYOTJEANNIN, C., with the technical collaboration of J. LE LAY & A. PAULIN. Au sujet de l'hypercuprémie des silicotiques. [**Increase in the Copper Content of the Blood in Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1959, July–Aug., v. 20, No. 4, 396–9.

In a study of 40 patients suffering from silicosis it was observed that generally there was an increase in the amount of copper in the blood serum [this *Bulletin*, 1959, v. 34, 904]. In the present work values of 160–190 μgm. per 100 ml. as against the normal 120 μgm. were found in men who drank large quantities of wine. To discover the factors leading to such increase the research was extended to a further group of silicotics, this time excluding alcoholics. Previous results were confirmed. The study showed that the increase was not related among other things to the inhalation of copper dust, heavy consumption of medicated red wines or domestic water supplies contaminated by solution of copper pipes. The authors submit that the increase of serum copper is a biological effect of the disease similar to other changes such as the increase of alpha and gamma globulins. *A. Meiklejohn*

LUPU, N. G., VELICAN, Doina, VELICAN, C. & OLINESCU, V. **The Action exerted by Certain Pneumoconiotic Factors upon the Acid Mucopolysaccharide Contents of Pulmonary Macrophages.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 244–7, 5 figs.

In studying experimentally the histochemical features in the development of fibrosis in pneumoconiosis Lupu and his co-workers observed that during the phase preceding the appearance of fibrosis metachromatic material and material positive to the periodic-acid-Schiff technique accumulates in the connective tissue interstices of the lung and this disappears almost completely after hyaluronidase extraction. To discover whether the mucopolysaccharide substance is secreted by pulmonary macrophages an experiment was conducted on 2 groups each of 30 guineapigs exposed to pure silicon dioxide and tobacco smoke. Concurrently observations were also made on post-mortem material of human lungs showing varying degrees of anthracosis.

Smears were made from all the collected lungs and stained with various dyes. Extraction was carried out with testicular hyaluronidase and the same cells were studied in comparative photomicrographs before and after enzyme treatment. The results showed that after the action of pneumoconiosis-producing agents the amount of mucopolysaccharides in pulmonary macrophages is significantly increased. During the initial phase of the appearance of these substances they are not extractable by testicular hyaluronidase. On the basis of these findings the authors submit that the increased amount of acid mucopolysaccharides in the connective tissue interstices of the lung during the phase preceding the onset of fibrous lesions is explained by the prolonged irritative action of pneumoconiotic substances, which they believe determine hypersecretion of acid mucopolysaccharides by the pulmonary macrophages. *A. Meiklejohn*

CRUICKSHANK, B. **Interstitial Pneumonia and its Consequences in Rheumatoid Disease.** *Brit. J. Dis. Chest.* 1959, July, v. 53, No. 3, 226–36, 11 figs. on 4 pls. [43 refs.]

Several lung lesions have been described in patients suffering from rheumatoid disease. The rheumatoid nature of rheumatoid granulomata and rheumatoid pneumoconiosis (Caplan's syndrome) are not questioned but necrotizing arteritis, sclerosis of the pulmonary arteries, focal arteritis, bronchiolitis, interstitial pneumonitis, diffuse interstitial pulmonary fibrosis and honeycomb lung are still controversial.

The object of the present report is to record 8 further examples of interstitial pneumonia, pulmonary fibrosis or honeycomb lung associated with rheumatoid disease and to assess the aetiology and pathogenesis of these changes.

The series comprised 4 males and 4 females in the age range 54–73. Case abstracts and pathological findings are detailed for each case. The features commonly noted were interstitial situation of the lesions, non-specific nature of the inflammation and fibrosis associated with bronchiolectasis. The cellular elements of the interstitial pneumonia were similar to those which occur in the synovial tissue and other inflammatory lesions of rheumatoid arthritis. There seemed to be a sequence of events. The first manifestation was a non-specific interstitial pneumonia, which is reversible at this stage and in which resolution probably occurs. This is followed by increasing fibrosis and bronchiolectasis of which honeycomb lung, localized or widespread, is the extreme form.

The aetiology of the lesions is discussed with particular reference to irradiation, systemic lupus erythematosus, diffuse acrosclerosis, polyarteritis nodosa and the Hamman-Rich syndrome. The conclusion is that the lung lesions are manifestations of rheumatoid disease. *A. Meiklejohn*

RUYSSEN. A propos d'un cas d'aspergillose et de suppuration broncho-pulmonaire caractérisé chez un ouvrier houilleur pneumoconiotique. [**Commentary on a Case of Aspergillosis and Bronchiectasis occurring in a Coalminer suffering from Pneumoconiosis**] *Arch. Malad. Professionnelles.* Paris. 1959, July–Aug., v. 20, No. 4, 446–8.

In 1950 a workman aged 60 years who had been employed from 1933–6 tunnelling in silica rock and thereafter to date underground in coalmines claimed compensation for silicosis. The radiograph showed bilateral fibrosis of the lungs but the medical board interpreted the lesions as tuberculous and disallowed the claim. He died 8 years later. At necropsy the lungs showed a moderate degree of silico-anthracosis together with suppurative bronchiectasis and multiple abscesses. The pneumoconiosis was confirmed histologically and *Aspergillus* was identified in the abscesses.

From the medico-legal aspect the question arises whether the death should be attributed to occupational or natural causes. Aspergillosis has been reported in association with coalworkers' pneumoconiosis but so infrequently that it can reasonably be regarded as an accidental superimposed infection. The relationship of the bronchiectasis to the pneumoconiosis is more difficult. Should it be regarded as an integral complication of the dust disease or as a concomitant but extraneous condition? Neither the relevant compensation law nor the experts in France apparently offer explicit guidance.

[The problem is not unique to France and it has troubled certifying experts in many countries. There is no definitive answer. The decision must depend on the accurately ascertained facts of the individual case. Where there is reasonable doubt, and the effective word is reasonable, then the claimant should have the benefit.] *A. Meiklejohn*

RAMSAY, J. H. R. & PINES, A. **Results of Treatment of Pneumoconiosis complicated by Tuberculosis.** *Brit. Med. J.* 1959, Sept. 5, 345–8. [25 refs.]

Chemotherapy has been highly successful in the treatment of uncomplicated tuberculosis but, as so far reported, it has little permanent effect in advanced pneumoconiosis with open tuberculosis.

Between 1953 and 1958, 25 patients, of whom 17 were suffering from coalworkers' pneumoconiosis with tuberculosis and 8 from silico-tuberculosis (all sputum positive), were treated by chemotherapy, PAS, streptomycin and isoniazid. The organisms in 24 cases were sensitive to all 3 drugs; the remaining case showed initial resistance to streptomycin. The radiographic pneumoconiotic changes were classified as simple in 7 cases and progressive massive fibrosis (PMF) in 18.

All patients were treated in hospital for a period of 1 to 12 months, the average stay being 8 months. Thereafter treatment was continued at home for varying periods.

In all except 1 who defaulted and another who relapsed temporarily the sputum became consistently negative, by smear and culture. Generally improvement in radiographic appearances was slight but more evident in cases complicating simple pneumoconiosis than in those associated with PMF. Though the general health of the patients improved, there was little change in exercise tolerance or capacity for work.

On the basis of this experience the authors conclude that patients suffering from pneumoconiosis with tuberculosis can be treated as successfully as those with uncomplicated tuberculosis. They ascribe the failures previously reported by others to incorrect use of chemotherapy. The article gives details of the schedules of treatment used.

[The number of patients in this series was small, which probably explains why the cases of coalworkers' pneumoconiosis and silicosis were not analysed separately. It is to be hoped that experience of similar treatment of larger groups of cases from coalmining and goldmining areas will enable comparison to be made of the efficacy of the treatment in the separate varieties of pneumoconiosis.] *A. Meiklejohn*

AMERICAN REV. RESPIRATORY DIS. 1959, July, v. 80, No. 1, Pt. 2, 1–213, 115 figs. [Numerous refs.] **Symposium on Emphysema and the "Chronic Bronchitis" Syndrome, Aspen, Colorado, June 13–15, 1958.**

Sponsored by the Colorado Tuberculosis Association, Colorado Trudeau Society, University of Colorado School of Medicine, Colorado Foundation for Research in Tuberculosis, National Tuberculosis Association and American Trudeau Society, the first Aspen symposium on emphysema and the "chronic bronchitis" syndrome was held at Aspen, Colorado, on June 13, 14, 15, 1958. 116 leading specialists including anatomists, pulmonary physiologists, pathologists, clinicians and veterinarians from United States, Canada and Australia attended.

In the foreword to this excellent volume of the proceedings Dr. R. A. PRINDLE, Chief of the Air Pollution Medical Program of the Public Health Service, Washington, D.C. concisely assesses the present situation:

> "Although pulmonary emphysema is a widely applied diagnosis, the condition itself is poorly understood and, even among the experts, there is lack of agreement on almost every point that would characterize the disorder anatomically, functionally and clinically. The need for a universally acceptable concept of pulmonary emphysema has become pressing in recent decades due to the increased incidence of the disease and the fact that it exhibits an ominous parallel to the progressive modernization of our environment.
>
> "To some, pulmonary emphysema is already a public health problem in America. Emphysema is, even now, a very serious matter in Great Britain, where it is a prominent feature of the chronic bronchitis syndrome [perhaps one might venture

to add pneumoconiosis] which has overtaken every other pulmonary disease as the foremost crippler and killer."

The Conference Steering Committee submitted 3 general purposes for consideration and deliberation by the conference:

"(1) To exchange information on the available knowledge and our lack of knowledge regarding the etiology and pathogenesis of diffuse obstructive pulmonary emphysema, . . . called 'emphysema';

"(2) to clarify terminology as it pertains to emphysema and related problems; and

"(3) to endeavour to stimulate interest and research into the etiology and pathogenesis of this obscure and common disorder."

In the opening paper R. S. MITCHELL (pp. 2–4) reviewed the many hypotheses of the pathogenesis of emphysema. By an almost endless series of questions he showed how little was known and how much remained undiscovered.

The anatomy of the lung was discussed in 5 papers, which covered the embryology, histology, pulmonary lymphatics and studies on collagen and elastin. [Considered as a whole these essays reveal the fascinating story not of archaeology and demolition but of masterly design and architecture.]

There were 4 papers on pathology. J. P. WYATT (pp. 94–103) stated that "the macrosection is the ideal way of demonstrating and producing an extremely informative morphologic map". He described in detail his own modification of the Gough-Wentworth technique for the preparations of these sections. Essentially the modification is that before full distension of the respiratory tree with formalin, the pulmonary artery and vein are injected with coloured latex.

C. S. HOUSTON, moderator of the physiology section (p. 114), states that 2 committees were appointed to recommend a definition of emphysema and to advise on the preparation of human lungs for macroscopic and microscopic study. These reports were not available in time for discussion at the conference but these with comments by experts are now printed. [These cannot be abstracted adequately and should be read in the original.]

The papers on physiology concentrated on the physics of air flow, mechanics of pulmonary ventilation and circulatory dynamics in pulmonary emphysema. Among the contributions on experimental studies, those on the experimental production of emphysema in laboratory animals merit attention. The symposium concluded with papers on the clinical aspects of emphysema.

In reviewing the arrangements and results of this first Aspen conference the organizers state that it is hoped to arrange an International Congress on emphysema in 1961, again at Aspen, Colorado.

[This volume should be in the libraries of all universities, medical schools, chest physicians and others interested in this and related fields of study. For 50 years radiology has dominated the study of the pneumoconioses; the leadership is now passing to the physiologists and pathologists.] *A. Meiklejohn*

STORSTEIN, O., FIELD, A. S., Jr., MASSUMI, R. & GRAY, F. D., Jr. **Airway Resistance and Lung Compliance. The Effects of Histamine and Hyperventilation in Normal Subjects and Patients with Chronic Lung Disease.** *Yale J. Biol. & Med.* 1959, June, v. 31, No. 6, 387–96, 3 figs.

"1. Lung compliance and airway resistance were measured in 17 normal subjects and 17 patients with various types of chronic lung disease both at rest and during hyperventilation before and after the injection of histamine.

"2. Compliance was in the low normal range for the patients with emphysema, but definitely low for patients with pulmonary fibrosis. Histamine and hyperventilation further lowered the compliance in the patients with emphysema, but had a less pronounced effect on the patients with fibrosis and in normal subjects.

"3. When airway resistance was low, compliance varied greatly, but when resistance was high, compliance tended to be low.

"4. Airway resistance was initially high in most of the patients. It increased following histamine injection and hyperventilation in most of the normal subjects and patients. Hyperventilation had a more pronounced effect than histamine."

GREENOUGH, G. K. **Wet Collectors of Respirable Dust for Use with Coal Mine Vacuum Cleaners.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield.] *Research Rept.* No. 156. 1959, Apr., 28 mimeographed pp., 12 figs. [27 refs.] [2s. 9d.]

2 types of wet dust collector are described for attachment to a powerful vacuum cleaner which could be used to clean up deposits of dust in coal mines. The use of a dry fabric filter is dangerous because a frictional spark might ignite methane given off by the collected dust and because of the risk of smouldering coal dust being sucked in and fanned into flame.

At the intake the dust concentration may be as high as 28 million particles per cm.^{3} (1,140 gm./m.^{3}). To reduce the effluent concentration below 400 particles per cm.^{3} requires a filtration efficiency exceeding 99·99% by number.

In the rotary wet collector which was tested air is drawn through an impeller rotating at a maximum speed of 3,000 r.p.m. while water is sprayed in at 100 lb. per square inch. Dust particles impinge on the wetted impeller and the dust-laden water drops which are flung off are collected in a cyclone.

The other collector consisted of a venturi into the throat of which water was sprayed through 4 radial holes.

In the particle size-range 0·5 to 5 microns the collection efficiencies measured for these devices were 84% to 87% respectively at power inputs of about 7 horse power per 1,000 cu.ft./min. It is possible that the venturi collector could be improved to some extent but the efficiencies are far below the order required for the vacuum cleaner. *C. N. Davies*

ANDRZEJWESKI, R. & MIKUŁA, K. Entstaubung industrieller Gase in einem rotierenden Entstauber "Zirkulator". [**A Rotary Dust-Extractor (Circulator) for Cleaning Industrial Gases**] *Staub.* Düsseldorf. 1959, May 1, v. 19, No. 5, 186–92, 11 figs. [11 refs.]

Dusty gas is admitted tangentially into a multi-bladed rotor, similar to that of a centrifugal fan; it is drawn through the blades against the radial pressure gradient and discharged along the axis. Suction is maintained by a centrifugal fan of larger diameter mounted in the same axle. The centrifugal force developed upon the whirling dust particles drives them radially outwards, against the air flow, to impinge on the containing wall from which they are directed into a hopper.

High efficiency of separation for sizes greater than 5 microns is claimed. The theory of operation is expressed mathematically and design data for circulators of different sizes are presented. *C. N. Davies*

REIF, E. Eine Methode zur Bestimmung von Staubkonzentrationen bei Bestäubungsversuchen. [**A Method of Measuring Dust Concentrations in the Laboratory**] *Staub.* Düsseldorf. 1959, June 1, v. 19, No. 6, 227–8, 4 figs.

The dust is sampled with a midget scrubber, which is claimed to be efficient for sizes down to 0·2 micron, and obtained as a suspension in liquid. The size distribution is performed on a drop of suspension in a blood counting cell under the visual microscope. The electron microscope can be used by allowing a drop of suspension to evaporate on the specimen holder.

Concentration is determined from observation of scattered light intensity in a compensation photometer, the calibration being obtained by weighing and dilution. *C. N. Davies*

SICHEL, H. S. **On the Size Distribution of Airborne Mine Dust.** Reprinted from *J. South African Inst. Mining & Metallurgy.* 1957, Dec., 171–213, 16 figs. [20 refs.] Discussion 213–25, 7 figs. & 1 diagram.

On the thesis that both the number concentration and the total surface area of the particles should be determined for airborne mine dusts the author sought for a size-distribution formula by means of which surface areas could be calculated in terms of parameters obtained by counting particles.

A study of mine dusts revealed that the number distributions were J-shaped and the surface areas were bimodal; these requirements were met by the formula:

$$dN/dx = A \exp(-\alpha \sqrt{x}) + B \exp(-\beta \sqrt{x}).$$

Finding that a considerable part of the surface area was contributed by relatively sparse large particles the author advocates counting over a larger area of the sample for coarse particles than for fine ones. A routine for performing such counts and evaluating the distribution constants is described. *C. N. Davies*

WHEATLEY, K. **Measurement of the Surface Area of Tridymite.** Reprinted from *J. Applied Chem.* 1959, Mar., v. 9, 159–62. [11 refs.]

Experiments with animals had shown that the rate of collagen production in lung tissue following the administration of quartz dust was increased if the dust had previously been etched whereas no change after etching was observed with tridymite dust.

Etching had also been shown to reduce the surface area of quartz and this, in conjunction with X-ray diffraction results, led to the supposition that quartz particles are normally covered with a surface layer of porous amorphous material which is removed by etching.

Work described in the current paper on tridymite dusts reveals no decrease in the surface area on etching and no change in the X-ray diffraction. It is concluded that, unlike quartz, tridymite is free from an amorphous surface layer and that collagen production in lung tissue is associated with the crystalline forms of silica.

A point which is not laboured in this paper is that both quartz and tridymite particles have been claimed to carry easily soluble surface layers, amounting to about 3% of the total weight for 2-micron particles, and that their solubilities are similar. There is, thus, a difficulty in identifying the soluble layer with the layer which gives amorphous X-ray diffraction and is removed by etching.

The specific surface measurements were carried out by nitrogen and krypton adsorption, by air permeability and by microscopy. A value for the surface area per atom of adsorbed krypton is obtained which is greater than the calculated value.

C. N. Davies

SCHLIPKÖTER, H. W., STEIGER, H., ESSER, H. F. & BECK, E. G. Elektronenoptische Untersuchungen von Grubenstäuben unter Verwendung von Membranfiltern. [**Electron Microscopic Studies of Mine Dust Precipitated on Membrane Filters**] *Staub.* Düsseldorf. 1959, Sept. 1, v. 19, No. 9, 320–22, 9 figs.

"The article points to the difficulties of the microscopical analysis of finest dusts and describes a method for the transfer of the dust precipitated on membrane filters on to electronic microscope slides. This simple method has stood the test with the analysis of dust-laden air underground and above ground. Several examples are cited and discussed."

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **The Pulmonary Response to Blast Furnace Stack Dust.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 197–204, 6 figs.

In the neighbourhood of blast furnaces at iron and steelworks and foundries the intermittent discharge of dense clouds of reddish-brown smoke from the tall chimney stacks is a familiar sight. Housewives complain that the iron smoke stains curtains and soft furnishings in their homes and by inference assert that it must affect their lungs. However, it is commonly

accepted by medical authorities that siderosis, even when the radiographic changes are gross, is a benign condition.

Dr. Gross and his co-workers obtained samples of a representative stack dust. Chemical analysis showed that the chief constituents were iron (76·03% as FeO_2), Si (8·72% as SiO_2), carbon (7·07%) and Al_2O_3 (3·33%). A quantity of this dust was reduced in particle size to an average of 1·7μ (surface mean diameter $=\Sigma nd^3/\Sigma nd^2$ and another portion was prepared in suspensions, average particle size 5·8μ.

A group of 30 rats were each given a single intratracheal injection of 30 mgm. of the fine dust and similar control groups were respectively given a like dose of almost pure kaolinite dust and quartz. 3 similar groups were given multiple doses amounting over a period to 230 mgm. of the larger particle dusts. The experiments covered a period of 18 months during which many of the animals, particularly in the quartz group, died from natural causes. The quartz produced severe dense silicosis but the kaolinite induced only a scant connective tissue reaction. By contrast the blast furnace stack dust, fine and coarse, provoked no discernible connective tissue reactions either in the lungs or lymphnodes. This would seem to classify this dust as even more inert than kaolinite, and as storage is almost exclusively in the air spaces, it has evidently a very limited power to penetrate the interstitial tissue of the lung.

[In Great Britain the Clean Air Act is directed to control and abate the pollution of the atmosphere by smoke from domestic, industrial and other sources.]

A. Meiklejohn

HORIUCHI, K., HORIGUCHI, S. & SUEKANE, M. **Studies on the Industrial Lead Poisoning. I. Absorption, Transportation, Deposition and Excretion of Lead. 6. The Lead Contents in Organ-Tissues of the Normal Japanese.** *Osaka City Med. J.* 1959, v. 5, No. 1, 41–70, 10 figs. [43 refs.]

This article deals with industrial lead poisoning only in so far as it is related to the normal metabolism of lead in human beings, with special reference to its deposition in foetal and adult tissues.

Tissues were obtained from autopsy and post-operative specimens of adults having had no overexposure to lead and from aborted or stillborn foetuses over the age of 5 months.

The samples of tissues and organs of adults—brain, lungs, heart, liver, kidneys, spleen, pancreas, stomach, intestines, bladder, uterus, ovary, thyroid, cutaneous tissue, spinal fluid, milk, bones, bone marrow and teeth —were made up to 15 to 20 gm., evaporated to dryness and ashed; teeth were decalcified. Foetal organs and tissues were similarly treated, as also were samples of placenta and umbilical blood.

Analyses were carried out by a modified dithizone mixed colour method. In adult tissues the highest concentrations were present in teeth (arithmetic mean 3,396 μgm. per 100 gm.), bone marrow (1,377 μgm.) and bones, particularly the femur (1,194 μgm.). The soft tissues and organs showed much lower values; bladder, fatty tissue and ovary none to a trace, kidneys and liver a moderate amount—kidneys average 140 μgm., liver 190 μgm.

Cerebrospinal fluid levels, with an average of 23 μgm. per 100 ml., were close to those of human blood, while milk contained only a trace to 12 μgm. The foetal tissues, with a distribution similar to that of adults, showed a lead content differing considerably from that recorded by many other observers—a maximum of 156 μgm. per 100 gm. of bone, for example, as compared with a value of 7,686 μgm. for rib by HANSMANN and PERRY (*Arch. Pathology*, 1940, v. 30, 226). These differences are attributed to the different methods used.

Placental tissue contained a maximum of 120 μgm. per 100 gm., and umbilical blood 90 μgm.

In order to determine whether there is a tendency for the lead content of the body to increase with age, correlation diagrams between age and lead content were made for soft tissues and bones. The soft tissue content bore no relation to age, but it appeared that that of bones does increase; in the femur the increase each year was estimated to be approximately 37 μgm. per 100 gm. This estimation confirms the assumption of other observers that in normal human beings who have not had excessive exposure to lead the slight amount absorbed is mainly excreted in the urine and faeces, a part being harmlessly deposited in the bones. Examination of the frequency distribution curves of the various organs and tissues after logarithmic transformation indicated that normal distribution usually follows the normal logarithmic type, but in two cadavers with a relatively large total lead content the greatest deviation was found in muscle and skin; it is suggested that in these two cases external factors of lead exposure must have played some part. The total body lead content of the Japanese of average constitution was calculated to be approximately 78 mgm. in adolescence and 131 mgm. in old age; the corresponding values in Americans have been reported as 100 to 400 mgm. for an adult, the difference being probably accounted for by differences in constitution, mode of life and food.

These results of analysis of foetal tissues, placentae, and umbilical blood indicate that lead passes from the mother through the placenta to the foetus, and it has been suggested by earlier workers in this field that long-term overexposure of the mother to lead may produce toxic effects in the foetus, but that since the lead content of bone increases with the development of the foetus at the expense of its blood content, bone tissue may have a protective function in this respect. *Ethel Browning*

OSHIMA, M. **[Studies on Lead Poisoning. Part 1. On the Daily Variation of Lead Quantity in Urine]** *Shikoku Acta Med.* 1959, May, v. 14, No. 5, 855–60, 3 charts. [14 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"Several times in the warm season (July to Sept.) and the cold season (Jan. to Mar.), a whole urine was taken during successive 2 or 4 days from a worker of a certain battery-reproducing plant. Each material was divided into three groups of morning, day time and

night, and the volume, specific gravity, quantity of lead and concentration of lead were determined.

"1) Concerning the daily variation of lead content of urine, the quantity of lead discharge (γ) should be more weighted than the lead concentration in urine ($\gamma/1$) which is influenced by the volume of urine. A caution also should be paid on the rate of lead discharge (γ/h).

"2) As the daily variation of lead content of urine is of large range, it will be needed to pay attention to any quantitative estimation of the lead in urine exclusively by the results of spot urine samples.

"3) Relatively large quantities of lead were discharged in urine of night groups.

"4) The lead concentration in urine showed a larger variation in the warm season than in the cold season.

"5) The correlation coefficient was found as follows, respectively: $\gamma = -0{\cdot}733$ between volume and specific gravity of urine, $\gamma = +0{\cdot}667$ between volume of urine and quantity of lead in urine, $\gamma = -0{\cdot}479$ between specific gravity of urine and quantity of lead in urine, and $\gamma = +0{\cdot}348$ between specific gravity of urine and lead concentration of urine."

PERNIS, B., BAIRATI, A., Jr. & GIUBILEO, M. Alterazioni delle emazie nel saturnismo sperimentale visibili al microscopio elettronico. [**Alterations induced by Lead in Red Blood Cells as observed with the Electron Microscope**] *Med. d. Lavoro.* 1959, May, v. 50, No. 5, 358–67, 5 figs. [Numerous refs.]

"Ultra-thin sections of erythrocytes and erythroblasts of guinea-pigs intoxicated with lead acetate have been examined at the electron microscope.

"Some of the circulating erythrocytes of the lead-poisoned animals showed the presence of swollen and altered mitochondria and/or of clusters of dense granules (diameter 50 ± 8 Å) with high electron scattering power (ferritin molecules). These erythrocytes are not reticulocytes and are not observed in the blood of control animals. These findings confirm those of BESSIS and BRETON-GORIUS (1957) on the erythrocytes of lead intoxicated rats.

"As it is known that lead interferes with the synthesis of heme and as it has recently been shown that many stages of this synthesis take place in the mitochondria it is believed that sub-microscopic alterations of mitochondria are the consequences of biochemical disturbances induced by lead."

SAVICEVIC, M., PETROVIC, L., STANKOVIC, M. & DJORDJEVIC, S. Prophylaktische orale Verabreichung von Ca_2EDTA (Mosatil-Bayer) bei Arbeitern, welche einer Vergiftung mit Blei ausgesetzt sind. 1. Teil: Verabreichung von 2g Ca_2EDTA pro Tag. [**Prophylactic Oral Administration of Ca_2EDTA (Mosatil-Bayer) in Workers Suffering from Lead Poisoning**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1959, Aug., v. 9, No. 8, 180–85, 5 figs. [23 refs.]

The therapeutic efficacy of EDTA compounds given intravenously in lead poisoning is generally recognized, but there is some difference of opinion with regard to oral administration, and still more as to its value by this route as a prophylactic measure. The amount absorbable by the oral route has been variously estimated at 2·6 to 18%, and it has been suggested that with long-continued administration enough copper and iron may be excreted with the lead to disturb the electrolyte balance. This investigation describes the effects of administration of 2 gm. daily for 40 days Ca_2EDTA in the form of tablets (Mosatil) on the symptoms, urinary excretion of lead and coproporphyrin, blood lead and punctate basophilia of 9 men suffering from lead poisoning; 8 others, who received no Mosatil, served as controls.

The main symptom mentioned is a "lead line"; this disappeared in 5 out of seven of the treated group; in the control group it remained unaltered. Muscle and joint pains were alleviated in the treated group. The urinary lead in the treated group rose to its highest level (average 1·4 mgm. per litre) during the first period of 10 days, falling during the second, reaching its lowest level (0·9 mgm. per litre) during the third, and rising to 1 mgm. per litre at the end.

The blood lead level fell during the first 20 days from 0·105 to 0·08 mgm.%, remaining near this level thereafter.

The coproporphyrinuria also showed a marked fall during the first 2 periods from 0·6 mgm. per litre to a final level of about 0·14 mgm per litre.

Punctate basophilia fell from an average of 1,300 to 400 per million during the first period, rising slightly again during the fourth. In the untreated group the initial values remained practically unchanged in all respects. The erythrocyte and haemoglobin levels showed no significant variation in either group.

It is concluded, on the basis of these results which show that oral medication with Ca_2EDTA in actual lead poisoning promotes the elimination of lead without any evidence of injury, that it would be an effective measure in prophylaxis also.

[The numbering of the Tables showing the curves of lead in blood and urine does not correspond with those given in the text.] *Ethel Browning*

FRIBERG, L. **Studies on the Metabolism of Mercuric Chloride and Methyl Mercury Dicyandiamide. Experiments on Rats given Subcutaneous Injections with Radioactive Mercury (Hg^{203}).** *Arch. Indust. Health.* Chicago. 1959, July, v. 20, No. 1, 42–9, 11 figs.

To compare the deposition of mercuric chloride with that of methyl mercury dicyandiamide and to study possible exchange reactions between the 2 compounds, 60 male rats were divided into series 1 and 2 and each series into 3 groups of 10, A, B and C. Series 1 were injected subcutaneously daily for 10 days with radioactive mercuric chloride, and Series 2 with radioactive methyl mercury dicyandiamide. For the next 16 days neither A group received any Hg, both B groups received the non-radioactive form of the mercurial given before and both C groups had an interchange, *i.e.* Series 1 C received the organic non-radioactive mercurial and Series 2 C the inorganic. 2 rats from each group were killed at intervals between the 11th and 26th days. 6 other rats formed Series 3; they were given the radioactive organic mercurial for 10 days and were killed on

the following day for immediate brain exsanguination by perfusion. The Hg dose was 1 mgm./kgm.

The loss of radioactive Hg from the 11th day onwards is shown in graphs as percentages of the average readings from blood and organs of animals killed on the 11th day, and by these illustrations Series 1 and 2 and the groups are compared.

Greater amounts of the Hg accumulated in the rats given the organic compound for 10 days than in those given the chloride, except in the kidneys: 100 times as much in blood, 10 times in cerebrum, cerebellum and brain stem—shown in the perfused animals not to be due to blood—10 times in speen and twice in liver. After the chloride, renal values were twice as high, with urinary excretion 20 times and faecal twice. Hg was more firmly bound when given in the organic form. Some exchange was demonstrated. In blood the organic mercurial inhibited the loss of the inorganic. [See also this *Bulletin*, 1958, v. 33, 141, 673.]

M. Patricia Fitzsimons

MONTANDON, A. Argyrose des voies respiratoires. **[Argyria of the Respiratory Tract]** *Arch. Malad. Professionnelles.* Paris. 1959, July–Aug., v. 20, No. 4, 419–21.

Industrial argyria, occurring in polishers, engravers and makers of artificial pearls, is known in two forms, cutaneous and ocular. In the cutaneous variety, the pigment is deposited in the sub-epithelial layer in the form of a practically insoluble albuminate of silver. In the ocular form the deposition is chiefly on the elastic fibres of the conjunctiva, more rarely on the lens, the vitreous body or the cornea.

Argyria of the respiratory tract is now described by the author in two men employed in the manufacture of silver nitrate; their only symptom was mild chronic bronchitis. There was no discoloration of the skin, eyes, mouth, pharynx, larynx or trachea, but the nasal fossae showed a bilateral symmetrical impregnation of both walls in the middle and upper region. In the more severe case bronchoscopy showed isolated plaques of pigmentation at the tracheo-bronchial junction and uniform zones of greyish-yellow coloration around the orifices of the smaller bronchi, the intermediate bronchi remaining free.

Biopsy of the nasal mucous membrane showed deposition in the sub-epithelial region; the basal membrane of the cylindrical epithelium and of the seromucous glands were heavily laden with particles of silver salts, which were also scattered in the mesenchyma and along the lymphatics. There was some evidence of phagocytosis by histiocytes.

The bronchial mucous membrane showed a deposit of silver in the basal membrane, but much less marked phagocytosis.

While this condition may be regarded as a form of pneumoconiosis, it differs from other varieties in that the silver particles are deposited as a suspension in vapour, not as dust, and in the absence of any inflammatory reaction or associated tuberculous or pre-tuberculous lesions.

It has a benign prognosis with no hazard of fibrosis and represents only a pigmentation comparable to that of anthracosis or siderosis. *Ethel Browning*

SUNDERMAN, F. W., DONNELLY, A. J., WEST, B. & KINCAID, J. F. **Nickel Poisoning. IX. Carcinogenesis in Rats exposed to Nickel Carbonyl.** *Arch. Indust. Health.* Chicago. 1959, July, v. 20, No. 1, 36–41, 6 figs. [11 refs.]

Rats which survived chronic nickel carbonyl poisoning which had lasted for 1 year [see this *Bulletin*, 1958, v. 33, 593] and others which survived a single near-lethal exposure were retained to observe whether tumours were induced. In some, pulmonary cancers developed after a latent period of 2 years or more; spontaneous pulmonary neoplasms occur only rarely in this species.

At the end of the second year after the initial exposures there were 6 survivors of 2 chronically poisoned groups, *i.e.* 5 of 64 exposed 3 times weekly to 0·03 mgm./litre and 1 of 32 exposed to double this amount; there were 3 survivors of 80 exposed once to 0·25 mgm./litre and there were 3 survivors of 41 controls exposed only to the vaporized alcohol-ether vehicle.

Among these 9 survivors, which died between 24 and 30 months after the beginning of the exposures to nickel carbonyl, 4 tumour bearers were found, 1 from each chronic group and 2 from the acute group. 24 months after the first exposure, the survivor of 0·06 mgm./litre died, followed shortly by 1 of the 0·25 mgm./litre survivors. In the lungs there were masses of adenocarcinoma, with squamous cell differentiation in some areas, and in the second rat also a greater degree of anaplasia; in the first, some alveoli were distorted by fibrous thickening with hyperchromatism of the epithelium, and in this animal there were renal and mediastinal metastases. The 0·03 mgm./litre survivor died after 27 months and had a small squamous cell carcinoma in the lung. The second survivor of the acute exposure was killed when moribund 30 months after exposure and had 2 small bronchial papillary adenomata. The other animals had no pulmonary tumours. *M. Patricia Fitzsimons*

SUZUKI, Y. *et al.* **[Studies on the Selenium Poisoning. Part 1. Effects of Exposure to Air Pollution on the Community Health in the Neighbourhood of a Selenium-Refining Plant]** *Shikoku Acta Med.* 1959, May, v. 14, No. 5, 846–54, 1 plan & 2 figs. [10 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The present report deals with the case that the processing of selenium-refining was revealed to have a detrimental effect upon the health of population in the neighbourhood of a plant, while the toxic effect of selenium has hitherto received scant attention from the viewpoint of industrial medicine.

"Hazardous articles discharged from the plant were estimated to be a selenium, lead or sulfur-dioxide. The content of each stuff of these three was measured respectively on the materials obtained from the plant to reveal the selenium to be the most significant object among them.

"It was also disclosed that selenium had been exhausted in the form of gas, pulverised dust or waste

liquid. There was an increase of concentration of selenium detected in the waste liquid and the soil of the neighbouring region. Over 0·1 ppm of selenium was found in 24% of urine specimens obtained from the inhabitants examined.

"However, there was no detectable increase of selenium content observed in drinking water, plants, farm products and the nails of the fingers and of the toes or hairs of the inhabitants.

"The majority of examined population of the village located in the vicinity of the plant exhibited both subjective and objective symptoms as considered suggestive of selenium poisoning.

"That is, the clinical pictures observed in these cases were as follows: 1) Yellowish or sallowish color of the facial skin. 2) Ridging or discoloration of nails of the fingers and of the toes. 3) Anemia in high degree. 4) Hypotension.

"It is the author's intention to proceed further studies on the distribution of selenium in food and soil in Japan."

MELVILLE, G. S., Jr., LEFFINGWELL, T. P. & HARTWIG, Q. L. **Effects of Site of Injection and Radiation on Toxicology of Didymium Nitrate.** *Arch. Indust. Health.* Chicago. 1959, July, v. 20, No. 1, 15–20, 5 figs.

Since in a reactor explosion it is inconceivable that a single element only would escape, the authors copied experiments in which they had used yttrium and lanthanum [see this *Bulletin*, 1959, v. 34, 465] with the mixture of rare-earth elements known as didymium. Didymium materials contained the oxides of lanthanum 45 – 46%, neodymium 32 – 33%, praseodymium 9 – 10%, yttrium only 0·4% and other elements. A solution of Di nitrate ($Di(NO_3)_3-_6H_2O$) was used for injection, and in wound healing experiments implanted sand was tested as well as Di nitrate in powder form, without and also with whole-body irradiation. Female rats were used for 30-day observations. The irradiated animals received 800 r ^{60}Co gamma rays.

Intraperitoneal injection of 21 rats with 400 mgm./kgm. resulted in 3 deaths on days 3, 5 and 9. 22 were injected 4 hours after irradiation and 20 died, 13 between days 2 and 6, 7 between days 10 and 13. This synergism of radiation and didymium was similar to results with yttrium and lanthanum alone, but the amount of yttrium here was too small to count. The contribution of other elements in the mixture is not known.

Subcutaneous injections were given of 160 mgm. of Di nitrate or Na nitrate in 0·8 ml. water or of 0·8 ml. 0·9% NaCl. The didymium rats developed local abscesses which discharged on day 10 and continued to do so. The other animals showed no abnormal signs.

Back incisions, 1 inch long, were impregnated with 400 mgm./kgm. of sand or Di nitrate and were clipped and sealed. Wounds in control irradiated rats and wounds impregnated with Na nitrate healed in 15 days. 4 of 8 rats with sand wounds and 4 of 7 with didymium wounds were irradiated. Though 2 of the irradiated animals with sand wounds died by day 13, all wounds were healing well by day 6 and healed completely, those in the irradiated animals more slowly. Until the 8th day the didymium wounds looked like the others, but then broke down and remained open; 2 irradiated animals died on days 9 and 21.

The effects of the less soluble oxides of the rare-earth elements, more likely in a reactor accident, are now being compared with those of the nitrate.

M. Patricia Fitzsimons

CAMPBELL, E. E. **The Determination of Zirconium in Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 281–3, 1 fig.

MINUTH, W. Über die Wirkung eingeatmeter Trichloräthylendämpfe und eingeatmeten Tabakrauchs auf das Blutbild des Kaninchens. [**The Effects of Inhaled Trichloroethylene Vapour and of Tobacco Smoke on the Blood Picture of Rabbits**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1959, Aug., v. 9, No. 8, 185–8, 6 figs.

Blood examinations were made of 3 rabbits exposed respectively to anaesthetic (Trichloran), ordinary industrial and impure industrial trichloroethylene, and of one rabbit exposed to the smoke of a lighted cigarette. For the trichloroethylene exposure the animals were placed for half an hour daily over a period of one month, and again after an interval of 3 months, in a cage containing a flask 12 cm. in diameter filled with trichloroethylene.

During the first period of exposure there was a fall in the total number of white cells and in granulocytes. The second period resulted in an initial rise of both, with a fall of lymphocytes; this was attributed to acquired tolerance to trichloroethylene, and was eventually followed by the leucopenia and granulocytopenia characteristic of the first period. The results were similar with all 3 varieties of trichloroethylene. Inhalation of tobacco smoke also produced a fall in total leucocytes and granulocytes with severe exposure, but when this was diminished by placing the animal in a larger cage both showed a rise, accompanied by an increase of eosinophils and basophils.

[The small number of animals used and the absence of any controls prevent the evidence from being entirely conclusive.] *Ethel Browning*

ALBAHARY, C., GUYOTJEANNIN, C., FLAISLER, A. & THIAUCOURT, P. Transaminases et exposition professionnelle au trichloréthylène. [**Transaminases and Occupational Exposure to Trichlorethylene**] *Arch. Malad. Professionnelles.* Paris. 1959, July–Aug., v. 20, No. 4, 421–6. [Refs. in footnotes.]

Abnormal amounts of the two varieties of serum transaminase (glutamic oxalacetic (SGOT) and glutamic pyruvic (SGPT)) have been recorded in certain liver disorders and are believed to be due to liberation of enzymes from the injured cells. Some authorities have found an increase in carbon tetrachloride poisoning.

Normal levels are given by the authors as 2–35 units for SGOT and 2–40 for SGPT, a unit corresponding to the formation of 1 μgm. of pyruvic acid liberated from 1 ml. of serum.

They have found a total level a little above normal in cases of cirrhosis of the liver, SGOT being chiefly

responsible for the increase. Normal levels were present in alcoholics not suffering from cirrhosis and in all but one of 12 workmen exposed to non-chlorinated aromatic hydrocarbons. In order to determine whether trichlorethylene has any effect on serum transaminase, examinations were made of 30 workmen exposed to concentrations below 100 p.p.m., all showing trichloracetic acid in the urine. Only 4 showed a transaminase level above the normal, and these deviations showed no correlation with other tests of hepatic function.

It is concluded that there are no early signs of severe liver disorder in trichlorethylene intoxication and that transaminase estimations are not of diagnostic value in trichlorethylene exposure. *Ethel Browning*

TORKELSON, T. R., WOLF, M. A., OYEN, F. & ROWE, V. K. **Vapor Toxicity of Allyl Chloride as determined on Laboratory Animals.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 217–23. [11 refs.]

——, ——, —— & ——. **Vapor Toxicity of Allyl Alcohol as determined on Laboratory Animals.** *Ibid.*, 224–9.

Allyl compounds are increasingly being used as intermediates in chemical synthesis.

In order to establish conditions safe for repeated exposure to these allyl compounds, essentially similar experiments were conducted with several animal species to determine the effects of prolonged inhalation of small amounts. Each article gives detailed descriptions of methods and results and also describes human sensory tests and precautions.

Allyl chloride, 3-chloro-1-propene; B.P. 45°C. In a pilot experiment with 8 p.p.m. (0·025 mgm./litre), 10 rats, 4 guineapigs and 1 rabbit were exposed 28 times for 7 hours a day on 5 days a week in a 160-litre glass chamber. Food and water were removed during exposure. A matched group underwent similar conditions without the toxicant. The chamber air was analysed satisfactorily by a method described.

Failing animals were killed for examination and the others were decapitated on the day after the last exposure. When judged by growth, behaviour, mortality, appearance and final body weights no ill effects were evident, but histopathological examination showed severe liver and kidney injury. Average spleen weights in female rats were less than controls.

In an experiment with 3 p.p.m. (0·009 mgm./litre) 24 rats, 3 rabbits, 9 guineapigs and 1 dog of each sex were exposed 127–134 times for 7 hours a day on 5 days a week during 180–194 days in a 3,700-litre vault-type stainless steel exposure chamber. The toxicant was delivered into the air stream of 340 litres/minute which entered the top, was evenly distributed by fan and was exhausted along the back and sides 6 inches from the floor. Analyses and monitoring were satisfactory. A matched group underwent similar conditions without the toxicant and another, not deprived of food and water remained in the animal quarters. The exposed dog had an eosinophilia of 10% and an increased spleen weight attributed to concurrent pneumonitis and a periarteriolar granuloma in the lung.

The only toxic effect was central lobular degeneration found in the livers of the female rats killed immediately but not in the recovery group; this suggests that with 3 p.p.m. there was no margin of safety.

10 of 13 volunteers reported odour but no irritation when exposed to 3 p.p.m. for 1–3 minutes in the vault chamber.

Concentrations injurious in short periods will be painful to eyes and nose, but sensory perception is no substitute for analytical control. Closed systems and respirators are advised. If spills occur the area should be evacuated and well ventilated. Eyes and skin should be protected from contact. Allyl chloride should not remain on the skin. Clothing should be removed if contaminated. Hands should be washed before eating or smoking.

Allyl chloride concentrations in air should be kept below 2 p.p.m. for 7–8-hour working, with a time-weighted average for all exposures not exceeding 1 p.p.m.

Allyl alcohol, 1-propene-3-ol ($CH_2 = CH\text{-}CH_2OH$); B.P. 96·9°C.

The pilot experiment with 7 p.p.m. (0·016 mgm./litre) produced liver and kidney injury, mild and reversible, like that from 8 p.p.m. allyl chloride but less severe.

The vault 6-month experiment with 2 p.p.m. (0·005 mgm./litre) resulted in no detectable injury.

5 of 10 volunteers perceived odour at 2 p.p.m. after 1–3 minutes. Precautions as above give greater emphasis to skin and ingestion hazards.

The maximum standard for allyl alcohol for 7–8-hour working should be 5 p.p.m. with a time-weighted average for all exposures not exceeding 2 p.p.m.

[See also this *Bulletin*, 1959, v. 34, 246.]

M. Patricia Fitzsimons

MAGOS, L. & SZIZA, M. Heinz-test képződés és hemoglobin-alteráció. **[Heinz-Body Formation and Haemoglobin Alteration]** *Egészségtudomány.* Budapest. 1958, v. 2, No. 4, 322–8, 2 figs. [48 refs.] English summary (7 lines).

Nitrobenzene was injected intraperitoneally into 21 white rats in a dose of 0·1, 0·2 or 0·4 cc. per kgm. In samples of blood withdrawn at intervals up to 168 hours, determinations were made of the content of total haemoglobin, methaemoglobin and verdoglobin by differential spectrophotometry, and of the number of Heinz bodies in blood films stained with crystal violet. The amount of methaemoglobin rose to 20–40% of the total haemoglobin by the 4th hour after injection and then declined steadily to very low values. The amount of verdoglobin rose after 4 hours to attain a maximum proportion of 4–5% after 48 hours and then declined slowly. Heinz bodies appeared in all animals after 24 hours in 70–100% of the red cells; the granules were fine at first, subsequently becoming coarse. The curves of the Heinz body counts showed a close parallelism with the curves of verdoglobin content, both rising in a similar manner after a latent period which coincided with the formation of methaemoglobin. *D. J. Bauer*

PERNIS, B. & BAIRATI, A., Jr. Osservazioni al microscopio elettronico sui corpi di Heinz. [**Electron Microscopy of Heinz Bodies**] *Med. d. Lavoro.* 1959, May, v. 50, No. 5, 351–7, 4 figs.

"Heinz bodies formation has been induced with phenylhydrazine in guinea-pig erythrocytes both *in vivo* and *in vitro*.

"These have been observed with Siemens Elmiskop 1 electron microscope after lysis with water and drying or after embedding in metacrylate and ultra thin sectioning.

"The Heinz bodies appear as round formations with a comparatively high electron scattering power; they are homogeneous and do not show any fine structure; they may or may not appear in contact with the erythrocyte cell wall.

"X-ray diffraction of isolated Heinz bodies supports their lack of any orderly crystalline or paracrystalline structure and is rather indicative (presence of a diffraction ring at 4·65 Å) for the presence of denaturated proteins."

PECORA, L. J. **Physiologic Study of the Summating Effects of Ethyl Alcohol and Carbon Monoxide.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 235–40. [22 refs.]

There are many reports in the literature of accidental poisoning in human beings, both at home and at work, stating that those who were known to have been drinking an alcoholic beverage before the accident generally experienced much more severe effects than the non-users of alcohol. Of the many toxic agents that have been reported to be potentiated by alcohol, carbon monoxide has received considerable attention in the last 15 years. The combination is of great interest because many people are exposed to varying levels of both substances daily while at work and in urban dwelling areas. The carbon monoxide concentration in streets in some large cities in the U.S.A. may reach 0·05%, which is five times the present maximum acceptable concentration.

12 mongrel dogs were used in these experiments and for 6 hours each day, 5 days each week for 21 weeks, 6 dogs were exposed to alcohol and carbon monoxide, 3 control dogs received alcohol alone and 3 received carbon monoxide alone. Alcohol was given in quantities by stomach tube to assure a level of about 0·15% in the blood in the dogs exposed to carbon monoxide and in the controls. The amount of alcohol given daily was approximately equal to 2 pints of table wine or eight bottles of beer (? pint bottles), and would be comparable to what a workman could conceivably ingest during a workday. The carbon monoxide level in the atmosphere of the exposure chamber was maintained at 0·01% by volume.

No significant summating effects of alcohol and carbon monoxide were noted in this study.

Bromsulphthalein liver function tests were carried out on alternate weeks but they were negative during the whole experiment. Electrocardiograms were made every two weeks on all the dogs and apart from certain minor irregularities were essentially normal. No observable neurological abnormalities were noted. Histological studies did not reveal any differences between groups nor were there any remarkable changes. A single electrophoretic assay of serum protein and lipoprotein during the last week of the experiment on all the experimental dogs and on a control group of normal dogs showed a marked decrease in total lipoprotein in the carbon monoxide group due chiefly to reduced beta fraction but this observation awaits confirmation from further studies.

The author remarks that there are other factors such as work load that could result in chronic anoxia which were not taken into consideration in this study, but which should be. *P. J. R. Challen*

AYER, H. E. & SALTZMAN, B. E. **Notes on Interferences by Oxides of Nitrogen with Estimations of Carbon Monoxide in Air by the NBS Indicating Tubes.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 337–9, 1 fig.

HAYES, W. J., Jr. **The Toxicity of Dieldrin to Man. Report on a Survey.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 5, 891–912. [11 refs.]

Indoor spraying with dieldrin for malaria control has increased in countries where workers are unaccustomed to using toxic chemicals and unlikely to cover the skin. Poisoning, sometimes recurring months after exposure, prompted the World Health Organization to send a toxicologist to observe antimalarial programmes in Kenya, Tanganyika, Iran, India (Bombay State) and Indonesia. His report shows that the hazard of this toxic substance is proportional to the degree of workers' exposure as determined by concentration of the spray, area of bare skin, duration of contact and lack of hygiene. It includes a review of the literature and recommendations which may minimize this calculated risk where dieldrin has become necessary because of resistance of some vectors to DDT.

A table compares spraying practices, exposure and incidence of poisoning in 11 programmes, the proportion of cases with fits varying from 47% to 100%. Poisoning has not occurred yet in the first 3 countries.

Dieldrin, dry or in solution, is easily absorbed by the skin, differing from DDT, and is only about one-half as poisonous by this route as by mouth. It is poisonous if inhaled but because of large particle size in wettable powders this is no hazard: "the spraying process does not grind the powder any finer".

Protective measures include: informing the worker of risk and measures, and supervision to ensure use; at least 2 sets of work clothes with high neck and long sleeves and trousers and also socks, shoes, a broad-rimmed water-repellent hat with a plastic veil where conditions prevent the use of a plastic face shield, and sometimes also a short plastic or cotton cape; frequent hand washing, face and hand washing before eating and smoking, immediate washing after recognized contamination and daily bathing and clothes washing after work—"to the toxicologist, there is always enough water for washing if there is enough for spraying"; if used properly, rubber gloves; handles for measuring and mixing equipment; sprayers, properly maintained, used at the lowest pressure for vector control; an 8-hour day and

40-hour week; food, water and tobacco protected from contamination.

A poisoned person should have no further contact, should be given a proper diet and barbiturates and be under medical supervision for at least 2 years. Information is needed on excretion rate, methods of measuring dieldrin in blood and excreta, relative absorption with different spraying conditions, and the relation between toxicity, dosage and time. *M. Patricia Fitzsimons*

Toivonen, T., Ohela, K. & Kaipainen, W. J. **Parathion Poisoning: Increasing Frequency in Finland.** *Lancet.* 1959, Aug. 22, 175–6, 1 fig.

Deaths from parathion poisoning in Finland have risen from 2 in 1952 to 105 in 1957. Of a total of 286 deaths, 237 were suicidal and there were 7 cases of homicide. Of the 42 accidental deaths, 27 occurred in the age group 0–9 years. In only 20% of cases had the victims access to parathion in their work. A stricter control of the sale of parathion in Finland is urged. [There is no reference to occupational poisoning from parathion in Finland.] *J. M. Barnes*

Kondritzer, A. A., Mayer, W. H. & Zvirblis, P. **Removal of Sarin from Skin and Eyes.** *Arch. Indust. Health.* Chicago. 1959, July, v. 20, No. 1, 50–52.

The conclusions from these experiments are that the eyes of factory and laboratory workers should be completely protected from splashes of this toxic water-miscible organic phosphate, and that flushing the skin with water 2 minutes after contamination would be effective.

Skin decontamination experiments were conducted on rabbits and guineapigs, the heads being protected from Sarin inhalation or ocular absorption. Liquid Sarin was applied to the abdominal wall, clipped the day previously, of the rabbits in 9 doses from 30 to 300 cmm./kgm. and of the guineapigs in 12 doses from 70 to 1,200 cmm./kgm. After 2 minutes the contaminated area was flushed slowly with 250 ml. cool water, the animal being tilted. After 4 hours these areas in survivors were swabbed with 5% Na carbonate solution and flushed with water. With rabbits the percutaneous toxicity of Sarin alone, in undecontaminated controls, lay between 6·6 and 29·8 times that of Sarin plus flushing. For the guineapig the percutaneous LD50 of liquid Sarin, 104 mgm./kgm., was three times that of the rabbit, but the species difference need not influence the view that flushing was effective, in that dosages of 6–8 times the percutaneous LD50 gave low mortality ratios.

Eye decontamination was tested in some 180 rabbits. Sarin diluted with water to give 12 doses between 16 μgm./kgm. and 50 in a volume of 0·01 ml./kgm. was applied to the cornea. After intervals of seconds the eyeball and socket were flushed with 6–10 ml. water. The results indicate that if the eye could be flushed even 1 second after a liquid Sarin splash the perocular LD50 of 35 μgm. would be increased only by a factor of about 6·2. A droplet of 3 mgm. may kill 50% of human beings. Assuming that 10–15 seconds are required for eye decontamination, the reduction in toxicity would only be 2-fold, and of little practical value.

M. Patricia Fitzsimons

Murphy, S. D. & DuBois, K. P. **Toxicity and Anticholinesterase Activity of Tributyl Phosphorotrithioate (DEF).** *Arch. Indust. Health.* Chicago. 1959, Aug., v. 20, No. 2, 161–6, 4 figs. [10 refs.]

S.S.S. tributyl phosphorotrithioate (DEF) is used as a defoliant on cotton plants and workers may come in contact with it during and after its application. The toxicity of DEF to laboratory animals is described. The LD50 to guineapigs, mice and rats ranges from 150 to 440 mg./kgm. and is similar after injection or ingestion. Signs of poisoning come on slowly but death from a single dose may occur up to 7 days later. Depression, weakness, inactivity and muscular rigidity might lead to laboured breathing and death from respiratory failure. Excessive irritation, salivation and lachrymation might persist for several days. DEF has a weak anticholinesterase activity determined *in vitro* but animals receiving repeated doses showed over 80% inhibition of brain cholinesterase activity but no signs of poisoning. The authors conclude that cholinesterase inactivation may account for some but probably not all of the signs of poisoning in animals. A similarity to the toxic effects of etrolene (O.O.dimethyl O-[2:4:5 trichlorophenyl] phosphorothioate) is noted. It is suggested that blood cholinesterase estimations should be useful in gauging exposure of workers who use DEF.

J. M. Barnes

Creasey, N. H. & Green, A. L. **2-Hydroxyiminomethyl-*N*-Methylpyridinium Methanesulphonate (P2S), an Antidote to Organophosphorus Poisoning. Its Preparation, Estimation and Stability.** *J. Pharmacy & Pharmacol.* London. 1959, Aug., v. 11, No. 8, 485–90, 3 figs.

Céspedes, R., Montero, J. V. & Sánchez, E. Intoxicación por hierbicida a base de dinitrofenol. [**Intoxication by Weed-Killer with a Dinitrophenol Base**] *Acta Méd. Costarricense.* 1959, Apr., v. 2, No. 1, 23–33, 12 figs. (9 coloured) on 3 pls. English summary.

This paper describes 4 fatal cases which have occurred during the last 5 years.

The reduction in the world price of coffee has caused the growers to adopt every possible means to reduce the cost of production and this includes an increasing use of weed-killers. The dinitrophenol weed-killer is applied in an oily solution or as a powder and it is absorbed by the mouth, the lungs and the skin. Gleason *et al.* (*Clinical Toxicology of Commercial Products. Acute Poisoning* (*Home & Farm*). 1957, Baltimore: Williams and Wilkins Co.) report that a dose by mouth of 1–3 gm. or one of 3 gm. spread over 5 days is fatal. There are no toxic effects in laboratory animals unless the temperature exceeds 16°C. and is humid.

The patients admitted to hospital had intense yellow stains on their hands and feet demonstrating that they had not used protective gloves and boots. The workers often fail, also, to use the masks which are provided.

The cases recorded were in the regional hospital at Turrialba, Costa Rica, which receives patients from a wide agricultural area. All had severe headache, profuse sweating, thirst, fatigue and fever which reached 41°C. within a few hours and in 1 case 43·5°C. In 3 of the 4 patients there were vertigo and vomiting and, in 1, neurological disturbances including loss of reflexes and disorientation. 1 patient suddenly became ill 15 days after his first contact with the weed-killer and died within 1½ hours. The length of illness in the others was 2, 7 and 23 days.

The post-mortem findings are given at length. In all, the yellow staining of hands and feet remained: the cerebrospinal fluid was yellow: there was congestion and oedema of the lungs with a muco-haemorrhagic exudate: yellow staining and small haemorrhagic foci were found in the lungs and in 3 cases throughout the gastro-intestinal tract. In all, the thyroid gland showed hyperplasia and there were haemorrhages into the suprarenals. The kidneys contained foci of necrosis with tubular involvement and the brains showed subarachnoid haemorrhages: in 2 there were punctate subpleural haemorrhages: in 1, blood in the intestines: in 2 the liver was enlarged and in 1 there were patches of necrosis. In all, the heart valves were yellow and there were subepicardial punctate haemorrhages.

Dinitrophenol stimulates metabolism, causes hyperfunction of the thyroid, increased oxygen demand and pyrexia. Death is due to circulatory and respiratory collapse which is preceded by anoxia, acidosis and dehydration.

Treatment consists in nursing the patient in a place where the temperature is below 16°C. and lowering the body temperature by cold damp sheets and cold enemata —not by drugs. Measures should be taken to deal with the dehydration and to restore the electrolyte balance. Gastric lavage and saline purgatives should be used when the poison has been ingested.

Prevention includes insistence on wearing protective masks, gloves and boots and limiting exposure by changes of work. The anaemic, the debilitated, the tuberculous and the diabetic should not be allowed to work in contact with the weed-killer and agricultural workers should be informed of the danger. *Allen Daley*

MATTHEWS, B. F. **Dermatitis in the South Wales Mining Industry: a Report of a Survey of Two Collieries.** *Brit. J. Indust. Med.* 1959, July, v. 16, No. 3, 200–207, 1 fig.

To determine the prevalence of dermatitis in collieries and to investigate the aetiology of the condition a survey was carried out at 2 pits in South Wales. The pits were selected on the basis of experience of compensation claims on account of dermatitis. At one applications were numerous—" high claim " pit—and at the other few—" low claim " pit. Total populations were respectively 1,017 and 1,074 and almost 100% were examined. The first stage was by a rapid screening—inspection and medical history—to discover all the men who were affected by skin disease. These were recalled or visited in their homes for intensive examination and investigation. Diagnostic criteria were defined and cases were classified into 3 groups, occupational, non-occupational and doubtful but possibly related to occupation. At the " high claim " colliery 71 cases of dermatitis were diagnosed, 29 occupational, 20 non-occupational and 22 doubtful; the corresponding figures for the " low claim " colliery were 73, 29, 21 and 23. The pattern at the two collieries was almost identical, suggesting that claims for benefit do not accurately reflect the prevalence of the disease. Further scrutiny indicated that the incidence of claims was related to the severity of the condition in the individual cases. The dermatitis most commonly affected the lower limbs and particularly so in coal-face workers. As to distribution of the cases the areas chiefly involved were those exposed to damage by friction.

A. Meiklejohn

CALNAN, C. D. **Allergy in Skin Disease.** *Postgraduate Med. J.* 1959, Aug., v. 35, No. 406, 445–50. [48 refs.]

JORDAN, H. S. & WELTY, C. G. **A Venturi Scrubber Installation for the Removal of Fission Products from Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 332–6, 3 figs.

Atmospheric Pollution

PHAIR, J. J., CAREY, G. C. R., SHEPHARD, R. J. & THOMSON, M. L. **Some Factors in the Design, Organization and Implementation of an Air Hygiene Survey.** *Internat. J. Air Pollution.* 1958, Oct., v. 1, Nos. 1/2, 18–30, 10 figs. (5 on 5 pls.). [25 refs.]

The paper reviews the experience gained during 3 pilot studies carried out in Cincinnati in 1955 and 1956 regarding morbidity surveys attempting to relate human reactions to the low levels of atmospheric contamination commonly found in urban areas of the U.S.A.

Each survey continued for 3 months, and involved detailed measurements of domestic and external environment simultaneously with subjective and objective assessments of the physiological state of selected groups of " cardio-respiratory cripples ". The subjects were selected on the basis of shortness of breath, residence in a smoky area, confinement to home and ability to keep a diary. Patients having allergic forms of asthma were rigidly excluded from the surveys. The inclusion of a

high proportion of subjects living in old peoples' homes and institutions was found to facilitate survey organization, although to minimize collusion patients were selected from a number of independent institutions.

The patients were visited 3 times weekly by practical nurses who checked entries, carried out lung function tests, and also serviced the environmental sampling apparatus. There was a fortnightly check, by one of the medical staff, of the techniques used by nurses and patients. Of the diary sheets, 3% were lost or spoiled by the patients, and 40% of the patients showed signs of diminution of accuracy of reporting during the 3-month survey period. The number of "lost" environmental observations due to mechanical failure of sampling apparatus, which was a serious problem in previous surveys, was materially reduced by having a technician on 24-hour call to attend to faults.

Physiological tests of lung function were selected on the basis of (a) simplicity, (b) reproducibility of results, (c) sensitivity in detecting changes produced by atmospheric contaminants, and (d) relationship to abnormalities of pulmonary physiology. Pulmonary pressure was measured by means of a simple aneroid gauge and plastic mouthpiece, and timed and untimed vital capacity by a McKesson-Scott bellows spirometer with Gaensler time-switch. A "box-bag" [this *Bulletin*, 1958, v. 33, 148] was found to be more portable and simpler to use than an oximeter for testing gas transfer aspects of pulmonary function.

Variations in environmental conditions between various parts of the city, and significant gradients between the inside and outside of domestic premises necessitated that subjects should be confined to one small section of the total city environment, and that continuous and accurate measurements must be made of the changes in this micro-environment, both internal and external. *D. E. Hickish*

LUCAS, D. H. **The Atmospheric Pollution of Cities.** *Internat. J. Air Pollution.* London. 1958, Oct., v. 1, Nos. 1/2, 71–86, 9 figs.

The atmospheric pollution of cities can be attributed not only to large industrial sources, but also to a large number of small sources such as domestic fires. In this paper, which should be read in full, the author derives an approximate formula for estimating city sulphur dioxide concentrations for specified rates of emission, wind speeds and size of city.

The author indicates that if concentrations are averaged over the normal range of wind directions, the concentrations of SO_2 produced at ground level by an area source such as a town are large compared with those produced by a single source. The worst pollution appears to occur about a mile downwind of the city centre, and pollutional levels decrease very rapidly outside the city boundary.

Application of the formula to the 1952 London fog leads to theoretical values for SO_2 markedly higher than those observed [this *Bulletin*, 1954, v. 29, 750] and it is suggested that under prolonged stable conditions the SO_2 is absorbed by fog droplets and oxidized or neutralized. A "time constant" of between 8 and 20 hours is indicated. *D. E. Hickish*

Hygiene of Buildings

HEAT REGULATION, VENTILATION AND LIGHTING

UNIVERSITY OF MICHIGAN. SCHOOL OF PUBLIC HEALTH. **Light and Vision.** pp. ii + 167, numerous figs. 1958. Ann Arbor: The Continued Education Service. 109, South Observatory Street, Michigan, U.S.A. [$5.00.]

The reviewer must confess to some disappointment with this publication, which is introduced as a "long overdue treatment of the subject of light and vision . . . designed to identify and illustrate in readily understandable terms the basic principles in these areas that govern seeing in various lighting environments, and to outline measures that will most effectively employ these principles in creation or adjustment of lighting environments to optimum conditions for seeing".

The book is the Proceedings of a 3-day course organized for industrial hygienists, public health personnel, school administrators, architects, and engineers, and is presumably directed at similar groups. It comprises 25 separate papers by different authors. It is surprising, therefore, that there is no concise description of the construction and function of the eye, such as that given by WESTON in his classic *Sight, Light and Efficiency*. Nor at the other end of the scale are there straightforward instructions on how to design a lighting system to provide the requisite standard of illumination as may be found in the British Lighting Council's booklet *Interior Lighting Design*.

The scientific section, which is reprinted from *Industrial Medicine and Surgery*, includes a report of research on the effects of poor illuminance on the oculomotor system, a description of a generalized method for specifying the interior illumination requirements of practical visual tasks on the basis of visual performance criteria, together with papers on visual comfort in factory and office situations, and the conduct of a lighting survey.

The remainder of the text is occupied by contributions of more discursive and practical nature dealing with the various types of light source available, maintenance of lighting systems, and lighting for specific locations. There is discussion of the parts to be played by the illuminating engineer and architect in the field of light and vision.

While in the opinion of the reviewer this volume does not fully achieve the professed aim, it does nevertheless include much that is of interest and value to those who have already had some introduction to the subject.

D. E. Hickish

Sanitation

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

SHAW, B. **Water in Rural Areas.** *Sanitarian.* London. 1959, July, v. 67, No. 10, 451–60, 4 figs.

This paper deals with the provision and improvement of water supplies in rural areas of the tropics; the author writes from Kenya. The subject is discussed under 3 heads: the improvement and protection of existing water supplies; the improvement of availability; and the provision of water where there was previously little or none. The ways in which these can be achieved are listed and discussed. It is unnecessary to comment on them in detail but it may be of value to mention certain cheap and practicable measures. Zoning as a means of reducing pollution can be made more effective by providing a stoned or concrete access point, and in small streams a dam may be built incorporating a delivery pipe or notch at the top. Springs are a purer source than streams and they can with advantage be piped to a storage tank holding more than 24-hour requirement which is delivered from taps. A description is given of a water supply from a furrow, which is filtered and stored.

Hydraulic rams have proved very successful provided they are given a little attention. They are of value only when the source provides at least 10 times as much water as is needed for delivery, but their advantage is that unskilled labour only is required for installation. The author has found small rams simpler to install than large ones and he recommends 2 4-inch rams in series where 1 of that size is not sufficient. Subsurface dams for seasonal rivers are mentioned. They trap water and silt, and the dam is progressively raised to a suitable height. The silt prevents evaporation and water is drawn from a concrete tube-well let into the silt and projecting above flood level.

[This is a very useful paper incorporating numerous practical points derived from the author's wide experience.] *T. H. Davey*

PEEL, C. **Water Supplies and Public Health in Tropical Africa.** *Sanitarian.* London. 1959, June, v. 67, No. 9, 406–14, 5 figs.

The problem of water supplies in tropical Africa, especially in Northern Nigeria, and the solutions available are described. The outstanding problems are acute shortage of water during the dry season in many areas and the generally low quality of supplies. It is calculated that on average one-quarter of the African woman's time is spent in obtaining domestic water. In some areas the dry season supply is stored in hundreds of earthenware pots in which *Aëdes* breeds happily. Rainfall wastage results from evaporation or from run-off due to deforestation, overstocking with cattle or shifting cultivation. Water conservation requires integration of many activities and should be organized at the highest governmental level and on a national scale.

The development of water supplies has been given a high priority on economic grounds and because they are a basic public health requirement. The installation of a village supply must not be regarded as an end in itself, but as the first step in a programme of environmental improvement. A piped supply is most popular but the water is often untreated and may become contaminated in the pipes. Underground sources tapped by wells provide a cheap and practicable supply but lifting the water is a problem. A rope and bucket causes contamination and manual pumps and water lifts usually break down. Wind-pumps have proved satisfactory in suitable areas in Northern Nigeria but they need skilled servicing. Where they are installed the well can be sealed over and the water pumped to an adjacent service tank. Large earthenware cisterns of about 3 million gallons capacity have been constructed in Nigeria in arid areas in order to conserve rain water during the dry season, and they have proved satisfactory. *T. H. Davey*

MEYER, R. Über einige Eigenschaften des Substrats, das den Salmonellenquotienten als Absterbequotienten im Grundwasser bedingt. [**On some of the Characteristics of the Substance in Underground Water affecting the Survival of Salmonella Organisms**] *Arch. f. Hyg. u. Bakt.* 1959, Aug., v. 143, No. 5, 334–47.

The question is discussed whether the death of salmonella organisms in underground water is due in the main to absence of nutritive factors or the presence of some lethal agent. The survival of inoculae of *Salm. typhi* and *Salm. paratyphi B* was estimated in samples of raw well water, after coagulation and filtration and from the water tower immediately before going into supply in the town of Aurich.

It is concluded that the deep well water contains an agent causing the death of *Salm. typhi* and *Salm. paratyphi B.* This substance resists boiling and is probably filtrable; it can be adsorbed on and eluted from ferric hydroxide, does not show any oligodynamic action and will inhibit the growth of the organisms in question when diluted with broth from 10^{-2} up to 10^{-4}.

E. Windle Taylor

WEIDMANN, S. M. & WEATHERELL, J. A. **The Uptake and Distribution of Fluorine in Bones.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 243–55. [18 refs.]

WEATHERELL, J. A. & WEIDMANN, S. M. **The Skeletal Changes of Chronic Experimental Fluorosis.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 233–41, 10 figs. (2 coloured) on 3 pls. [22 refs.]

BLACK, A. P., LACKEY, J. B. & LACKEY, Elsie W. **Effectiveness of Iodine for the Disinfection of Swimming Pool Water.** *Amer. J. Pub. Health.* 1959, Aug., v. 49, No. 8, 1060–68.

The investigation described in this paper was undertaken to study the effectiveness of iodine for the disinfection of swimming pool water. Chlorine has certain

disadvantages and iodine is acquiring increasing importance as a disinfectant in a variety of fields. "Several novel and effective iodine preparations" are now on the market and also the price of iodine has come down to an economic level.

In the work recorded here 8 swimming pools ranging in capacity from 33,000 to 500,000 gallons and in daily bathing load from 3 to over 1,700 persons were studied by methods of sampling and chemical and bacteriological tests which are described. Iodine was added to the pool water as potassium iodide with some iodine-releasing material such as a small amount of chlorine or as a solution of iodine in potassium iodide.

The results of the study which are described with tabulated data led to the conclusions that:—(1) when compared on the basis of halogen residuals iodine was not only equal to chlorine but in many cases superior to chlorine, (2) the desired iodine residual could be maintained with a much smaller applied dosage than was true of chlorine, (3) iodine residuals appear to be much less dependent on bather load than do chlorine residuals, (4) these studies indicate that a daily dose of 1·0 p.p.m. of iodine is adequate for small pools and perhaps double that figure for more heavily used public pools, (5) about 0·2 p.p.m. of residual iodine should provide water of satisfactory quality, (6) no odours, tastes or irritation of the eyes of bathers were produced, (7) no visible algal growths were noted and (8) no brown iodine colour was observed when the iodine was uniformly distributed.

M. E. Delafield

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

McGauhey, P. H. & Klein, S. A. **Removal of ABS by Sewage Treatment.** *Sewage & Indust. Wastes.* Wash. 1959, Aug., v. 31, No. 8, 877–99, 10 figs.

In a 4-year programme of research the effects of alkyl benzene sulphonate [ABS] without fillers, on a laboratory scale, on the processes of sewage treatment have been investigated by these authors.

The ABS was determined chemically by the methyl green method or radio-assayed when AB^{35}S was used. A radioactivity balance in the activated sludge experiments was not possible owing to the loss of volatile intermediates.

The type of solids present, rather than the concentration of solids, accounted for large differences in ABS adsorption while ABS present in concentrations normally encountered in sewage would not hinder the sedimentation process.

Between 2 and 4% of ABS was removed by primary settling, 10–12% ABS being associated with the solids (accounts of 30% removal by primary settling must be based on faulty analytical methods, the authors state).

In batch-scale activated sludge experiments of 48-hour detention period 70% ABS was removed, about one-half of this disappearing in the first 4 hours of aeration. Sludges developed on synthetic sewage were found to be less efficient at removing ABS than those fed with domestic sewage *i.e.* (25% removal–54% removal with 6 p.p.m. ABS present). ABS removal was found to be more efficient at high solids concentration (5,000–6,000 p.p.m.) than low concentrations. The aeration rate had little effect on ABS removal and the first signs of toxicity (*i.e.* a decrease in the efficiency of ABS removal) were evident at 20–25 p.p.m. ABS.

An ABS balance for the laboratory activated-sludge experiments was suggested as:

ABS Status	%
Removed by sedimentation	3
In plant effluent	53
As intermediate degradation products	37·4
As final degradation products	6·6
Total	100

Modifications in activated-sludge plant to remove ABS were suggested and tried out in the laboratory.

The second stage of a 2-stage activated-sludge unit removed only 1% of the ABS applied to it, but broke down the intermediates of ABS degradation to sulphate.

In a 2-stage activated sludge unit with the second stage receiving added BOD as raw sewage solids, 25% of the influent ABS was removed.

A high-rate filter (5 ft. x 6″) removed 25% of applied ABS and this efficiency was not affected by increasing the recirculation ratio from 3:1 to 9:1, although the efficiency of the filter in terms of BOD-removal increased.

Surface stripping of induced froth was suggested as an intermediate or tertiary process if it was required to remove a greater percentage of ABS than was possible by the activated sludge process. By induced frothing 80–90% ABS removal was feasible, the froth being burned with waste digester gas. *D. Jenkins*

Infestation and Disinfestation

Wharton, R. H. & Abu Hassan Bin Omar. **The Effect of House Spraying with Dieldrin on the Incidence of the Head-Louse,** *Pediculus humanus capitis. Med. J. Malaya.* 1959, Mar., v. 13, No. 3, 237–8.

Observations of Busvine and Reid in 1949 indicated a high incidence of head lice in Malay schoolgirls; 57% of the girls examined were infested [see this *Bulletin*, 1950, v. 25, 163].

In 1954 it was noted that in villages in which the houses were sprayed with dieldrin against mosquitoes, the girls were found to be free of lice; whereas in a nearby unsprayed area, 37 of 57 (65%) were infested. A further examination was made in June 1958 in one village sprayed regularly for 4 years, one sprayed for

1 year and one unsprayed locality. Boys were examined as well as girls. In both treated villages no lice were found, but a few girls had nits which appeared to be hatched or dead. In the unsprayed village 19/30 boys and 52/58 girls had nits and 17/30 boys and 24/58 girls had live lice. (The percentage of lice in the boys is higher, probably because they are easier to detect, by combing, in short hair.) *J. R. Busvine*

BROWN, W. B. **The Disinfestation of Furniture with Methyl Bromide for Control of the Bed Bug.** *Sanitarian.* London. 1959, June, v. 67, No. 9, 403–5.

Disinfestation of furniture by hydrogen cyanide for bed bug control is still practised to some extent. This paper reports on dosage, toxicity and technique of use of methyl bromide which has been recommended since it is less dangerous. After preliminary trials in a steel fumigation chamber with various concentrations of methyl bromide operating for various periods (the concentration of toxicant x number of hours of exposure = c.t.), tests were made on a mixed load of furniture and bedding in a fumigation van at 21°C. with a c.t. of 110 oz.h.per 1,000 cu. ft., the gas being injected through a jet and distributed by a desk fan.

The dose of methyl bromide recommended, a c.t. product of about 150 mgm.h. per litre for temperatures around 15°C., is given by 32 oz. per 1,000 cu. ft. allowed to act for 5 hours. Though the period of exposure is longer than in the case of cyanide the subsequent airing period is greatly reduced so that treatment takes about the same time. The risk to operators is greatly reduced, respirators are not considered necessary, and the range of furniture and bedding which can be treated is greater than with cyanide. Infestation with the furniture beetle, *Anobium punctatum,* or with the common clothes moth can be treated in the same way.

[See also *Trop. Dis. Bull.*, 1957, v. 54, 1024.]

T. H. Davey

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

NUTTING, L. A., LOMOT, P. C. & BARBER, F. W. **Estimation of Coliform Bacteria in Ice Cream by Use of the Membrane Filter.** *Applied Microbiol.* Baltimore. 1959, July, v. 7, No. 4, 196–9.

The membrane filtration of melted vanilla ice cream was improved 5–20 times by the addition of Triton X-100. It was also improved by the addition of gelatin or sodium alginate as stabilizer during manufacture. M-Endo-MF medium proved satisfactory for the detection and enumeration of coliform organisms, in a series of 22 known strains, including Gram-positive cocci for differentiation. Comparative counts by the membrane filter technique and the deoxycholate lactose agar plate method gave similar results, and the recovery of coliform organisms by membrane filtration was at least as good as for deoxycholate lactose agar.

Similar results were obtained for coconut, peach, and strawberry ice cream, but chocolate ice cream presented difficulties due to particle size of the chocolate. The method eliminated interference from sucrose and consequent false-positive reactions. *Betty C. Hobbs*

ANDERSON, W., BURTON, L. K. & CROOKALL, J. O. **Current Trends of Strontium-90, Strontium-89 and Caesium-137 Levels in Milk.** *Nature.* 1959, July 11, v. 184, 89–91, 2 figs. [14 refs.]

"It is widely recognized that milk is an important proximate source of the long-lived fission products present in the human body." In a recent communication (*Nature*, 1958, v. 182, 1473) "the main information available on the levels of radiostrontium and radiocaesium occurring in milk produced in Great Britain" was summarized. The present article "reports detailed experimental observations" on the levels of strontium-90, strontium-89, and caesium-137 occurring in milk produced in west Cardiganshire (Felinfach Creamery) throughout 1958.

The values obtained monthly in 1958 for the levels of these 3 nuclides are set out in figures and a table with clear description of the variations in these levels with reference also to the levels in herbage and rain-water determined by other workers. There is expert discussion of these levels and of their trend in relation to rate of fall-out and cumulative fall-out, with reference also to the detailed accounts which have been published on the world-wide deposition of long-lived fission products.

"It is not possible to forecast accurately the levels of strontium-90 and caesium-137 which will occur in milk during the current year, since neither the 1959 rainfall nor the influence of the 1958 series of weapons tests on the specific activity of the rain can be exactly predicted. Provided that no further testing occurs, the levels of strontium-89 in milk produced after the summer of 1959 might be expected to be less than one-tenth of the levels occurring during November 1958." *M. E. Delafield*

FOOD POISONING

BROOMHEAD, C. L. & MANN, P. G. **A Family Outbreak of Salmonella thompson Infection.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, July, v. 18, 124–7.

6 persons suffered from vomiting and diarrhoea and one person from nausea only, 4–20 hours after eating tinned oranges garnished with a whip prepared from gelatin, sugar and the whites of several hen eggs. Salm.

Thompson was isolated from one or more samples of faeces from each of the 7 affected persons. 12 eggs from a flock of young Thornber Hybrid pullets were examined in groups of 4 and Salm. Thompson was isolated from one group. The birds had just begun to lay but were passing bulky mucus-laden stools. Of 9 blood samples, 6 showed O agglutinins to *Salm. thompson* at 1/40 but no H agglutinins. Chicken meal, droppings, and more eggs were examined but no other source of infection was found. The birds were treated with nitrofurane for 2 weeks.

No evidence of infection was found in a second flock of poultry consisting of 47 birds about one year old which were crosses between Black Leghorns and Rhode Island Reds, kept in an adjoining run; the fowl houses of the two flocks intercommunicated. *Betty C. Hobbs*

GRAHAM, J. M., PAYNE, D. J. H. & TAYLOR, E. **Salmonella Irumu Infection indirectly associated with South African Frozen Egg.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, July, v. 17, 176–7.

"A small outbreak of food poisoning due to *Salmonella irumu* is recorded. The evidence suggests that a food handler was infected through handling contaminated South African frozen egg and, in turn, infected a meat product which was responsible for the outbreak.

"The importance of close co-operation with the Salmonella Reference Laboratory in this outbreak is stressed, as the epidemiological information supplied gave the vital clue to the origin of the outbreak."

COOPER, E. D. **An Acute Outbreak of Staphylococcal Enterotoxin Food Poisoning.** *South African Med. J.* 1959, June 27, v. 33, No. 26, 542–5.

220 of 290 persons were taken ill, some as early as 1–1½ hours after eating lunch at a club house in Cape Town during a bowls tournament. Vomiting, prostration and collapse were predominant symptoms. There were no deaths. All except 2 persons had eaten cold tongue or corned beef which had been cooked and cooled on the premises. *Staphylococcus pyogenes aureus* was recovered, not only from the tongue and corned beef, but also from fresh cream eclair, ice cream, pickled herring, strawberries, French salad, beetroot soup and butter, and also from brine used by the butcher who supplied the beef. It is interesting to note the wide dissemination of the organism, *via* the preparation tables and hands of the kitchen staff to almost every article of food used at the function.

The kitchen was unsatisfactory for the provision of large numbers of meals and refrigeration facilities were limited so that the hot cooked corned beef and tongue were left to cool in a hot pantry.

The necessity for rapid and effective cooling of all foodstuffs retained for subsequent use is emphasized.

The coagulase-positive staphylococci responsible for the outbreak were of phage type 29 which does not seem hitherto to have been implicated as a cause of food poisoning. The same type was found in nasal swabs from a member of the kitchen staff. Food poisoning is not a notifiable illness in South Africa.

Betty C. Hobbs

HOUSTON, T. M. **Food Poisoning due to Clostridium Welchii.** *Pub. Health.* Johannesburg. 1959, Apr., v. 25, No. 1, 33–42. [10 refs.]

An outbreak is described in which 10 of 15 people were taken ill with pain and diarrhoea some hours after eating cold chicken from a packed lunch on a warm day. Heat-resistant *Cl. welchii* were isolated from the chicken, from 3 of 4 samples of faeces from patients and from 2 of the kitchen staff responsible for the preparation of the picnic lunch. The poultry had been boiled in a large container, transferred to other containers and allowed to cool in the liquor before being transferred to the refrigerator. Poultry prepared in a similar manner had caused illness on a previous occasion. The methods of slaughtering and marketing the poultry were investigated.

It is emphasized that the introduction of cooking techniques which eliminate anaerobic conditions favourable to bacterial growth is as important as the identification of carriers, and is a practical measure in the prevention of this type of food poisoning.

Betty C. Hobbs

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

HABEEB, A. F. S. A. **A Study of Bacteriological Media: The Examination of Casamin E.** *J. Pharmacy & Pharmacol.* London. 1959, Aug., v. 11, No. 8, 496–500, 1 fig. [18 refs.]

"Three batches of Casamin E have been examined quantitively for their free and total amino acid content. Variation occurs in the free amino acid content in the three batches examined. The peptides were examined qualitatively. The batches were examined for their strepogenin activity using the media of Steele, Sauberlich Reynolds and Baumann and Kodicek and Mistry. The stimulatory pattern appeared to be different with the two basal media."

[See this *Bulletin*, 1959, v. 34, 557.]

EIDUS, L., DIENA, B. B. & GREENBERG, L. **Observations on the Use of Tetrazolium Salts in the Vital Staining of Bacteria.** *Canadian J. Microbiol.* Ottawa. 1959, June, v. 5, No. 3, 245–50. [11 refs.]

Vital staining of bacteria with 4 tetrazolium salts was studied to determine concentrations for optimal staining and for complete inhibition of bacterial growth. The salts employed were neotetrazolium chloride (NTC), triphenyltetrazolium chloride (TTC), blue tetrazolium (BT) and nitro-blue tetrazolium (NBT). Experiments were carried out in liquid medium to which were added various concentrations of the salts. Organisms used were several species of mycobacteria including BCG and chromogenic strains, a selection of members of the Enterobacteriaceae, Gram-positive rods and cocci. TTC was found to be the least toxic salt and the greatest amount of dye was taken up at a concentration of approximately 50% of the toxic level.

Microscopic examination showed that NTC penetrates the cell walls, is reduced to both a reddish and a purple formazan, and stains internal structures. Acetone washing fails to decolorize the cells. Studies with BT and NBT salts were limited to mycobacteria and the organisms were uniformly stained. TTC acts differently from the other salts. It does not penetrate the cells of mycobacteria but is reduced on the surface and crystals of formazan may be seen. Gram-positive and Gram-negative organisms take up the salt and form large deposits of formazan internally. Acetone washing for 12 hours fails to decolorize Gram-positive cells but Gram-negative bacteria are decolorized in 20 minutes. Autoclaved, dead bacteria are unstained by these salts but after exposure to ammonium sulphide fumes, organisms become coloured, showing that dead cells may absorb the salt but are incapable of reducing it to formazan. *May F. McCallum*

AMBLER, R. P. & REES, M. W. **ε-N-Methyl-Lysine in Bacterial Flagellar Protein.** [Correspondence.] *Nature.* 1959, July 4, v. 184, 56–7, 1 fig.

ARMSTRONG, J. J.; BADDILEY, J.; BUCHANAN, J. G.; DAVISON, A. L.; KELEMEN, M. V.; NEUHAUS, F. C. **Teichoic Acids from Bacterial Walls. [i] Composition of Teichoic Acids from a Number of Bacterial Walls** [ARMSTRONG, BADDILEY, BUCHANAN, DAVISON, KELEMEN & NEUHAUS]. *Nature.* 1959, July 25, v. 184, 247–8. [ii] **Structure of Teichoic Acid from the Walls of** *Bacillus subtilis* [ARMSTRONG, BADDILEY & BUCHANAN]. *Ibid.*, 248–9. [14 refs.]

BERRY, L. J.; SMYTHE, Dorothy S.; YOUNG, Leona G. **Effects of Bacterial Endotoxin on Metabolism. I. Carbohydrate Depletion and the Protective Role of Cortisone** [BERRY, SMYTHE & YOUNG]. *J. Exper. Med.* 1959, Sept., 1, v. 110, No. 3, 389–405, 2 figs. [49 refs.] **II. Protein-Carbohydrate Balance following Cortisone. Inhibition of Intestinal Absorption and Adrenal Response to ACTH** [BERRY & SMYTHE]. *Ibid.*, 407–18. [17 refs.]

MORTON, J. J. **The Struggle against Sepsis.** *Yale J. Biol. & Med.* 1959, June, v. 31, No. 6, 397–422. [177 refs.]

A review.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order:—General; Antibiotics; Other Therapeutic substances; Disinfection.

ANDRISCHOCK, H. O. &. BOESE, W. Diffusionstest oder Röhrchentest? [**Diffusion Test or Tube Test?**] *Arch. f. Hyg. u. Bakt.* 1959, June, v. 143, No. 4, 287–304, 19 figs. [23 refs.]

The sensitivity of multiple strains of various bacteria to 5 antibiotics and 2 antibiotic mixtures was tested by 2 methods. For the diffusion test "a few loopfuls" of a young broth culture of the organism were placed on a blood agar plate and uniformly spread: filter paper disks containing antibiotics were placed on the surface; the plate was refrigerated for 4–5 hours to permit diffusion before growth and then incubated for 10–20 hours. Strains showing any inhibition zone around a disk were then tested against that antibiotic by a tube dilution method. For this 2-fold dilutions were made starting with broth containing 2·5 mgm./ml.: there were 10 dilutions, the last thus containing 4·5 μgm./ml. To these tubes, each containing 5 ml. medium, was added 1 ml. of (apparently undiluted) broth culture of the organism. The tubes were read for turbidity after 20 hours' incubation to determine the inhibitory concentration and plated to determine the bactericidal.

The results are presented by plotting inhibition zone diameter against minimum inhibitory and bactericidal concentrations. There are 19 such diagrams, and with few exceptions they show many gross discrepancies: in some instances organisms showing an inhibition zone of, *e.g.* 2·4 cm. diameter gave results in the tube dilution test covering the whole range of dilutions, some strains not being inhibited by the highest concentration and others inhibited by the lowest. These diagrams give the results of tetracycline, streptomycin and penicillin + streptomycin against staphylococci, streptococci and *Escherichia coli*, chloramphenicol and neomycin against these 3 organisms and *Proteus*, and erythromycin against staphylococci and streptococci only. The only series of tests not exhibiting these gross discrepancies was that with neomycin. The authors conclude that diffusion tests are unreliable, and although affording preliminary information, should be followed by a tube dilution test. [They do not mention ever having repeated a test giving a widely discordant result, and they seem to have made no effort to find an explanation for it. It is impossible to suggest one, both because the discrepancies are so enormous, and because innumerable technical details are omitted: there is even no mention of the quantities of antibiotics in the disks. The inoculum in the tube dilution test was so large that it must itself have produced

some turbidity in all the tubes. The lowest concentration in this test, 4·5 μgm./ml., is much greater than the minimum inhibitory concentration of some of these antibiotics for some of the organisms as ordinarily determined. There are no illustrations of any cultures.] *L. P. Garrod*

DAVIS, I. **Rapid Hemoglobin-Reduction Method of determining Microbial-Antibiotic Susceptibility.** *Med. Technicians Bull. Suppl. to U.S. Armed Forces Med. J.* 1959, May–June, v. 10, No. 3, 131–4, 2 figs.

A thin layer of 20% blood agar is poured in plates. This is covered with a layer of 0·25% glucose agar or other appropriate medium with which the inoculum has been mixed. Antibiotic disks are placed on the surface. Growth reduces the haemoglobin in the lower layer, producing a colour change which is absent from any inhibition zone. Such a zone is said to become visible in only 2 hours. [The inoculum is described as either a culture or a clinical specimen. A warning might have been advisable that if the specimen contains 2 or more organisms, only one of which is the cause of the infection, the method may be misleading.] *L. P. Garrod*

MIAN, K. A. **Microbial Sensitivity Test in Management of Urinary Tract Infections.** *J. Amer. Med. Ass.* 1959, June 20, v. 170, No. 8, 934–8, 2 figs.

This is one of several recent papers proposing the reduction of haemoglobin as an indicator of growth in a rapid sensitivity test. The basal layer in a 15 cm. Petri dish is 20 ml. of a special medium prepared from ox heart, calf brain, potato, peptone and dextrose, + 3 ml. horse blood: 5 ml. of the same medium is inoculated with centrifuged deposit of urine and poured over the first layer: finally antibiotic disks are placed on the surface. Inhibition zones produced by them retain the colour of oxyhaemoglobin, which elsewhere is reduced by bacterial growth. The result can usually be read in 5 hours: curves are reproduced showing the frequency with which the test can be read at different times, and the dependence of this on the size of the inoculum. Very satisfactory clinical results were obtained from treatment directed by this test. [The author does not say what antibiotics were used, or how much of them the disks contain, although he does say that "2 concentrations of each therapeutic agent were used with respect to the Gram-reactions of the organisms." He also says that they "can be used again", a somewhat surprising suggestion, both because they are liable to be contaminated, and because this type of test assumes that the whole of the antibiotic in the disk will diffuse into the medium.] *L. P. Garrod*

VAICHULIS, E. M. K. & DOLL, J. P. **Instability of Penicillin in Dubos Media.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 262–3. [20 refs.]

"The Dubos broth base medium with the addition of oleic-albumin complex destroys penicillin relatively rapidly. Dubos broth base medium with the addition of the albumin complex slowly destroys penicillin during an incubation period of seven days. Dubos media are unsuitable for ascertaining the true susceptibility of *M. tuberculosis* to penicillin, unless accurate determinations are made to establish the amount of active penicillin remaining in the medium."

BANIC, S. **Transduction to Penicillin and Chloramphenicol Resistance in** *Salmonella typhimurium*. *Genetics.* 1959, May, v. 44, No. 3, Pt. 2, 449–55.

"An aerated broth-culture method as well as a double-agar-layer technique were worked out by which it is possible to transduce sensitive strains of *Salmonella typhimurium* by first-step and multistep penicillin- or chloramphenicol-resistant mutants. Multistep resistant mutants are capable of transducing sensitive strains only to a degree of resistance corresponding to first-step resistance. This means that separate genes controlling resistance to penicillin or to chloramphenicol are not linked. Transduction of first-step penicillin-resistant strains by independent first-step mutants gives rise to second-step resistance. These data confirm the hypothesis that a polygenic system governs multistep resistance."

BARDI, U. & DI MARCO, A. Ossidazione di prodotti terminali del metabolismo dei carboidrati in ceppi di *Escherichia coli*, sensibili e resistenti alla streptomicina. **Oxidation of Terminal Products of Metabolism of Carbohydrates in Strains of** *E. coli* **Sensitive and Resistant to Streptomycin**] *Giorn. di Microbiol.* Naples. 1958, July–Dec., v. 6, Nos. 1, 2 & 3, 103–10, 5 figs. [15 refs.] English summary.

LINZ, R. Irradiation par les ultraviolets et résistance d'un colibacille à la tétracycline. [**Ultra-violet Irradiation and Resistance of a Colibacillus to Tetracycline**] *C.R. Soc. Biol.* 1959, v. 153, No. 2, 373–6.

A strain of *Escherichia coli* was habituated to tetracycline on gradient plates, so that it grew normally on medium containing 2·5 μgm./ml. and poorly on 50 μgm./ml. A suspension was submitted to ultra-violet irradiation for 1, 3 and 6 minutes, at the end of which period there were very few survivors. After each period the suspension was plated on medium with and without 2·5 μgm./ml. of tetracycline, and in each pair of cultures the number of colonies was about 10 times greater on tetracycline-containing medium. This difference persisted after 30 minutes' cultivation in broth, but was lost after 24 hours. The author confesses inability to explain this effect. *L. P. Garrod*

KURYŁO-BOROWSKA, Zofia. **Antibiotical Properties of the Strain** *Bacillus brevis* Vm4. *Bull. Inst. Marine Med. Gdańsk.* 1959, v 10, Nos. 1/2, 83–98, 8 figs. [10 refs.]

A soil sample from the Mazury lake region yielded an antibiotic-forming strain of *Bacillus brevis*. This paper deals chiefly with cultural conditions for the production

of this antibiotic and the use of counter-current distribution in its extraction. It has been only partially purified: some physical and chemical properties of the product are given. In simple diffusion tests of capacity to inhibit growth it shows activity against both Gram-positive and Gram-negative species: its absolute activity cannot be deduced because concentrations are expressed in " units ", without reference to weight. The relationship of this substance to known antibiotics formed by *B. brevis* is not discussed. [In a brief catalogue in the text of previous studies in this field the work of Dubos is mentioned last. Is the author really unaware that Dubos not only isolated an antibiotic from *B. brevis* for the first time, but in showing that it could exert a systemic therapeutic effect, laid the foundations for all modern antibiotic therapy?] *L. P. Garrod*

COURTIEU, A. L., BERTOYE, A. & LONGERAY, C. Sensibilité à la ristocétine de quelques souches microbiennes. [**Sensitivity of Certain Bacterial Strains to Ristocetin**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 417–19.

The English summary appended to the paper is as follows:—

" Study of 169 strains belonging to various genera and species. The antibiotic is active on Gram-positive germs, particularly on streptococci, enterococci and *Listeria.* It has no activity on Gram-negative bacteria, even on *Neisseria.*"

[See this *Bulletin*, 1958, v. 33, 976.]

FUNK, A. & DIVEKAR, P. V. **Caerulomycin, a New Antibiotic from** *Streptomyces caeruleus* **Baldacci. I. Production, Isolation, Assay, and Biological Properties.** *Canadian J. Microbiol.* Ottawa. 1959, Aug., v. 5, No. 4, 317–21, 2 figs.

" *Streptomyces caeruleus* has been shown to produce a hitherto unknown antibiotic to which the name caerulomycin has been given. This was first obtained from a fresh isolate (PRL 1687), and subsequently, after the strain had been identified, from an authentic culture of *S. caeruleus.* It was extracted from culture filtrates with ether and purified as a colorless crystalline amphoteric substance, $C_{12}H_{11}O_2N_3$, which inhibited the growth of some filamentous fungi and yeasts and had weak activity against certain bacteria."

MURAI, K., SOBIN, B. A., CELMER, W. D. & TANNER, F. W. **PA-108, PA-133A, PA-133B, and PA-148: New Macrolide-Type Antibiotics. I. Chemical Characterization.** *Antibiotics & Chemotherapy.* New York. 1959, Aug., v. 9, No. 8, 485–90, 1 fig. [10 refs.]

" Three new macrolide-type antibiotics, PA-108, PA-133 (A and B), and PA-148, have been isolated from different strains of *Streptomyces.* Purification procedures, criteria of homogeneity, and physicochemical properties are reported for the homogeneous elaboration products."

PÉNAU, H., HAGEMANN, G. & VELU, H. Sur l'activité antibiotique d'une souche nouvelle de *Streptomyces.* [**The Antibiotic Activity of a New Strain of** *Streptomyces*] *Bull. Soc. Chimie Biol.* 1959, v. 41, Nos. 5/6, 761–5, 1 fig.

The English summary appended to the paper is as follows:—

" The cultures of a new strain of Streptomyces produce two biologically active substances; one of them shows a high inhibitory activity toward gram-positive and gram-negative bacteria, the other has an interesting antifungal property. The basic antibacterial substance, isolated from the culture filtrates: ' Antibiotic 4915 ', or ' Hydroxymycine ', has a broad spectrum of activity, and is less toxic than Neomycin."

WOODSIDE, R., ZIEF, M. & SUMRELL, G. **The Antibacterial and Antifungal Activity of Thiol Esters.** *Antibiotics & Chemotherapy.* New York. 1959, Aug., v. 9, No. 8, 470–74.

" A series of aliphatic and aromatic thiol esters has been synthesized and tested against bacteria and fungi in vitro. The two most active antibacterial and antifungal thiol esters prepared were *p*-chlorophenyl thiol methacrylate and *p*-chlorophenyl thiol furoate."

GILLESPIE, E. H. & ROBINSON, W. **Blanket Laundering and Sterilization. Report of a Trial at the City General Hospital, Sheffield.** *J. Clin. Path.* 1959, July, v. 12, No. 4, 351–4.

It is now generally accepted that hospital blankets can be a potent source of cross infection, and that they should be disinfected at frequent intervals. 2 practical methods of achieving this have been suggested. Wool blankets can be disinfected by incorporating a disinfectant rinse in a low temperature laundry process or blankets can be made from materials which will withstand a temperature high enough to kill vegetative organisms. The choice of methods will, in fact, depend on cost, convenience to nursing staff and acceptance by patients.

This paper describes a comparison of 4 types of blanket, wool untreated (weight 5 lb. 2 oz., cost 53s. 10d.), wool treated against shrinkage (5 lb. 2 oz., 61s.), cellular cotton (loom state) (3 lb. 6 oz., 29s. 11d.), and Turkish towelling (5 lb. 4 oz., 66s. 6d.). The wool blankets were washed in a non-ionic detergent, followed by a quaternary ammonium compound rinse. The cotton and towelling blankets were washed at 160°–170°F. and 180°–200°F. respectively in an alkaline solution containing an anionic detergent and pure soap, followed by a cold rinse. Blankets were washed up to 15 times, and were compared for general condition, shrinkage and convenience in use. Their bacteriological state was examined by the " sweep plate " method of BLOWERS and WALLACE [this *Bulletin*, 1955, v. 30, 897].

The bacteriological results were uniformly satisfactory. Before laundering, counts of from 300 to " uncountable " were obtained—afterwards they were of the order of 5, with no pathogens.

After 15 washings the untreated wool blankets showed some felting and dullness of colour, the treated ones were

"of good appearance and in moderately good condition". The cotton blankets were quite satisfactory, although a shrinkage of up to 10% was found. This could largely be prevented by stretching during the laundry process. They were popular with nurses, who found them easy to handle in bedmaking, and with patients, who found them light but warm. They were also cheaper than the other blankets. They had a tendency to cause "fluff" but this gradually ceased with use. The towelling blankets withstood laundering well but were unpopular as they were difficult to handle, and were heavy but not so warm.

The authors recommend that cotton blankets be purchased in future, and that where existing stocks of wool blankets must be used, a disinfectant stage should be included in the laundry process. There is a useful discussion of the whole problem. *J. C. Kelsey*

WALTER, C. W. & KUNDSIN, Ruth B. **Faulty Function of Table Model Ethylene Oxide Sterilizer.** *J. Amer. Med. Ass.* 1959, July 25, v. 170, No. 13, 1543–4.

The authors tested a table model ethylene oxide sterilizer of approximately 1 litre capacity, using a "single shot" container to inject 12 gm. of a mixture containing 20% ethylene oxide. Ambient temperature and humidity were used, and a 2-hour exposure was recommended. Tests were made with suture loops, cotton wool pledgets and stainless steel strips. The pledgets were contaminated with *Clostridium sporogenes*, the other 2 objects with *Bacillus subtilis*. Positive results were obtained from each after as much as 4 hours' exposure with the sutures and strips and 2½ hours with the pledgets. It is concluded that the method recommended is obviously not safe and suggested that the rate of kill would be greatly increased by raising the temperature and that the relative humidity should be controlled at about 28%.

[It is this sort of finding that makes workers in Britain reluctant to recommend the use of ethylene oxide sterilizers in hospitals or elsewhere, except in circumstances where the initial formulation of operating procedure and its day-to-day implementation can be checked by adequate bacteriological controls.] *J. C. Kelsey*

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes; Leptospira; Anaerobic; Bacillus; Others.

VAN OYE, E. Les Salmonelloses humaines au Congo belge et au Ruanda-Urundi: Statistiques sur 1000 cas. [Miscellanea.] **[Human Salmonelloses in the Belgian Congo and Ruanda-Urundi: Statistics on 1,000 Cases]** *Acta Tropica.* Basle. 1959, v. 16, No. 2, 158–65. [15 refs.]

The reports on the distribution of the different salmonella sero-types in various parts of the world are always interesting although figures indicating frequency of occurrence of certain sero-types can be of doubtful significance unless each isolation or identification reported refers to an incident which may have involved a single sporadic case or an outbreak involving even hundreds of cases. This report coming from the laboratory at Léopoldville does not appear to be unaffected by these reservations. For instance, to report that of the 1,000 cultures of salmonellae examined 74 were found to belong to a new sero-type, Salmonella Kisangani (1, 4, 5, 12; a; 1·2), could indicate a wide distribution of this organism throughout the area or a single incident involving 74 or more individuals. On the other hand it is of considerable epidemiological interest to know that Salm. Thompson, a very common salmonella type in the Far East, was not found in this area of Africa.

From the information that can be extracted from this report, it would appear that typhoid fever is very common in the area, that paratyphoid fever is relatively uncommon and that salmonellosis is widespread. Out of 1,000 salmonella cultures examined, which were exclusive of *Salm. typhi*, there were 106 different sero-types. *Salm. typhi-murium, Salm. enteritidis,* Salm. Dublin and *Salm. paratyphi C* accounted for some 500 of the cultures. When the 74 cultures of Salm. Kisangani are added to this total it can be seen that relatively few of the remaining 101 sero-types could have been associated with any large outbreak of disease. The report is of interest because it is a further illustration of the very wide variety of salmonella sero-types that can be found in tropical areas. *H. J. Bensted*

TAYLOR, W. I. & SILLIKER, J. H. **Isolation of Salmonellae from Food Samples. III. Dulcitol Lactose Iron Agar, a New Differential Tube Medium for Confirmation of Microorganisms of the Genus** *Salmonella. Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 335–8, 2 figs.

In the course of more than 150 isolations of naturally occurring salmonellae, more than 95% gave the correct reactions in the dulcitol lactose iron agar contained in one tube as described in the paper. Exceptions were one dulcitol negative Salm. Worthington, and a few H_2S negative strains of various sero-types.

The only atypical coliform bacilli producing characteristic salmonella reactions belonged to the Ballerup-Bethesda paracolon group which could be differentiated by the ninhydrin test.

The medium is claimed to be superior to the Kligler iron agar and triple sugar iron agar slants because the use of a carbohydrate less frequently fermented by organisms not of the salmonella group than glucose was thought to be an advantage, and also the butt reaction was not obscured by excess H_2S. The medium is stable at room temperature: acid and gas are shown in the butt of the tube by fermentation of dulcite. Formation of H_2S is shown as a black rim around the centre of the medium, and the reaction of lactose is shown in the slant. [See also this *Bulletin*, 1959, v. 34, 808.]

Betty C. Hobbs

KELEMEN, G. Transductios kísérletek a *Salmonella* csportban. [**Transduction Experiments in the *Salmonella* Group**] *Egészségtudomány. Budapest.* 1958, v. 2, No. 4, 310–16, 1 fig. [27 refs.] English summary.

In transduction experiments with an O strain of *Salmonella paratyphi B* of antigenic structure 1, 4, 5, 12:— it was possible to induce flagella formation by transduction of the antigens b, 1, 2 and i from a phage of *Salm. typhi-murium* and the induced character was found to be heritable. In a similar manner the gm flagellar antigens could be transduced by a phage of *Salm. enteritidis* to give a recombinant strain with the antigenic structure of Salm. Essen; the same result could also be obtained with a phage from Salm. Essen. The transduced variants retained the ability to form a mucoid wall and were susceptible to lysis by the transducing phage. A variant with the antigenic structure of Salm. Sendai was similarly obtained from *Salm. enteritidis* and a phage of *Salm. paratyphi A.* *D. J. Bauer*

CZERNIAWSKI, E., SEDLACZEK, L. & ZABŁOCKI, B. **Properties of Antigen O of *Salmonella typhi* in relation to Culture Media.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1958, v. 6, No. 7, 287–91, 1 fig.

A number of different liquid and solid culture media were compared in respect of the yield and quality of the O antigen when they were used to grow typhoid bacilli. It was found that the yield of O antigen obtained from organisms grown on liquid media was inferior to that obtained from solid media cultures; beef or liver extract agars gave the best results. The amount of polysaccharide in a particular batch of O antigen did not depend on the amount of reducing substances in the media and there was no correlation between total N in the antigen and total N in the culture media. Liver extract agar medium yielded an O antigen which was much more toxic to white mice than antigens obtained from organisms grown on beef extract, plus egg or serum, agars. Moreover the liver extract O antigen in precipitation tests with homologous antiserum gave titres many times higher than antigens obtained from growths on other media and this was confirmed when the gel precipitation pattern was examined. *H. J. Bensted*

RZUCIDŁO, L., KUBICA, J. & BIEL, J. **Chemical Structure and Biological Properties of the Cellular Residue of *Salmonella typhi*.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1957, v. 5, No. 12, 425–9.

It is already known that substances can be extracted from the cell walls of certain fungi, mycobacteria and corynebacteria and also some coliform organisms which can significantly influence the pathogenicity of other bacteria (*Staphylococcus aureus, Salmonella typhi*) when injected intraperitoneally into mice with such strains. There was no information, however, available about the biological properties of the isolated cell wall, or its extracts, of *Salm. typhi* and this paper is concerned with experiments for their determination.

The authors employed a phenol extraction method for the preparation of cellular residues of 5 strains of *Salm. typhi*. Chemically the residue of the cell walls was found to consist mostly of protein. The total N in the residues of the 3 strains tested varied from 1·22–1·40 mgm. per 10 mgm. of the material. Paper chromatography identified the same amino acids in all five strains and indicated traces only of one saccharide—probably glucose. The almost complete absence of saccharides, the high total N and the ease by which the cellular material was hydrolysed showed the chemical structure to be different from other bacteria examined. When the biological properties were examined it was found that none of the different strain-suspensions was toxic for mice and, mixed with just sub-lethal doses of *Staph. aureus,* only one strain appeared to enhance the pathogenicity of the inoculum and that was by no means definite. It would seem therefore that the isolated cell wall of *Salm. typhi* does not contain any substance with the same properties as zymosan (from *Candida*) or similar toxic reagents which have been isolated from the cell wall of other organisms. *H. J. Bensted*

MATĚJOVSKÁ, Věra & JELÍNEK, J. K otázce fagotypizace *S. typhi.* [**The Phage-typing of *S. typhi***] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 3, 168–72. [12 refs.] English summary.

The authors present the results of the phage-typing of 6,557 strains of *Salmonella typhi* carried out between 1949 and 1958 in the Institute of Epidemiology and Microbiology in Prague. The most frequent types were E1, D1, F1, A, C and D4, and G, D2, D5, B1, F2, M, N and T were also encountered. Of 40 E1 strains examined further with VII phage 37 were of subtype a. 75% of 5,600 strains were of biotype I, including most of the E1, F1, D1, C and D4 strains. *D. J. Bauer*

RAETTIG, H. Provokation einer Infektion durch Schutzimpfung. 2. Mitteilung. Unspezifische Provokation während der experimentellen Epidemie mit *S. typhi-murium.* [**The Provocation of an Infection by Vaccination. 2. Non-specific Provocation during Experimentally Produced Epidemic Conditions with *Salm. typhi-murium***] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 3/4, 236–44, 2 figs. 3. Mitteilung. Schutzimpfung in einem endemisch verseuchten Mäusevolk. [**3. Vaccination of an Endemically Infected Mouse Population**] *Ibid.*, 245–57, 5 figs. [10 refs.]

2. The effect of following up oral infections with *Salmonella B. typhi-murium* by subcutaneous injection of killed suspensions of the same organism have already been described [this *Bulletin*, 1959, v. 34, 1164].

In extension of this work, the effect of vaccination with (a) closely related organisms, *i.e. Salm. enteritidis jena* and *Salm. enteritidis kiel* and (b) bacteria with widely divergent antigenic characters, *i.e. Escherichia coli* (mixture of 4 strains) has been studied. The extent of provocation of latent infection has been found to be greatest with the homologous bacteria, less so with the more nearly related strains and least perceptible with the *E. coli* strains.

3. The conclusion suggested in the previous communication that infection may be promoted by protective

inoculation is open to the objection that the artificial massive infection to which the mice were subjected does not correspond to anything that occurs in the natural development of epidemics. 2 further lines of investigation have therefore been pursued. The first was to observe the influence of protective inoculation of groups of mice on the emergence of latent infection. Several groups of mice ranging between 100 and 300 were divided up into batches of animals inoculated with heat killed *Salm. typhi-murium* vaccine and controls. In one of these groups an unexplained infection, probably a pneumonic virus infection, in a second a Dansyz enteritidis and in a third a *Salm. typhi-murium* infection occurred and in every case the mortality in the vaccinated group exceeded or markedly exceeded that in the control group.

The second line of investigation was to introduce an infected mouse into a healthy community and then proceed to vaccinate a portion of the group after 5 days or longer, the period being varied with the susceptibility of the breed of mice.

The result was as before, the mortality in the vaccinated group was always greater.

The practical suggestion is made that an injection of heat-killed *Salm. typhi-murium* vaccine to a selected group from a larger number of mice is the best method of determining the presence of latent infections in a collection of mice.

The experiments are claimed to provide evidence of the dangers of artificial immunization of human beings while an epidemic is already under way.

J. W. McLeod

OZEKI, H. **Chromosome Fragments participating in Transduction in** *Salmonella typhimurium*. *Genetics*. 1959, May, v. 44, No. 3, Pt. 2, 457–70, 2 figs. [22 refs.]

BUXTON, A. **The** *In Vivo* **Sensitization of Avian Erythrocytes with** *Salmonella gallinarum* **Polysaccharide** *Immunology*. Oxford. 1959, July, v. 2, No. 3, 203–10. [15 refs.]

LE MINOR, L., THOME, M., PERREAU, P. & CHARIÉ-MARSAINES, C. Deux nouveaux sérotypes de *Salmonella*: S. Millesi (40:lv:1,2) et S. Tchad (35:b:-). [**Two new** *Salmonella* **Serotypes: S. S. Millesi and S. Tchad**] *Ann. Inst. Pasteur*. 1959, Sept., v. 97, No. 3, 406–7.

The English summary appended to the paper is as follows:—

"Isolation of two new *Salmonella* serotypes in the Tchad region, from bovine nodes."

LE MINOR, L, EDWARDS, P. R, MILLE, R. & DRÉAN, D. Un nouveau sérotype de *Salmonella*: Salmonella Quinhon (47:z44). [**A New** *Salmonella* **Serotype: S. Quinhon.**] *Ann. Inst. Pasteur*. 1959, Sept., v. 97, No. 3, 407–8.

The English summary appended to the paper is as follows:—

"Description of a new *Salmonella* serotype, *S. quinhon* (47:z44) isolated from lizards in Vietnam. Its flagellar antigen is a new H antigen possessing antigenic relationships with *z* of *S. poona* phase 1."

NÉEL, R., LE MINOR, L. & CHARIÉ-MARSAINES, C. Un nouveau sérotype de *Salmonella*: S. Spartel (21:d:1,5). [**A New** *Salmonella* **Serotype: S. Spartel**]. *Ann. Inst. Pasteur*. 1959, Sept., v. 97, No. 3, 409.

The English summary appended to the paper is as follows:—

"Description of a new *Salmonella* serotype, *S. spartel*, isolated from a grass snake, and characterized by the formula 21:*d*:1,5."

RAMSEY, Carolyn H. & EDWARDS, P. R. **Two New** *Salmonella* **Types: Salmonella Holcomb and** *Salmonella* **Newrochelle.** *Internat. Bull. Bact. Nomencl. & Taxon.* 1959, July 15, v. 9, No. 3, 111–12.

"Two new *Salmonella* serotypes are described: *S. holcomb* (6, 8: 1, v-e, n, x) and *S. newrochelle* (3, 10: k-1, w). Both were isolated from cases of enteric infection in man."

MORAN, Alice B. & EDWARDS, P. R. **A New** *Salmonella* **Type: Salmonella Escanaba (6,7: k-e,n,z_{15}).** *Internat. Bull. Bact. Nomencl. & Taxon.* 1959, July 15, v. 9, No 3, 113–14.

"A new *Salmonella* type, *S. escanaba* (6, 7: k-e,n, z_{15}) is described. It was isolated from the stool of an asymptomatic adult female who had diarrhoea one month previously."

BARON, L. S., SPILMAN, W. M. & CAREY, W. F. **Hybridization of** *Salmonella* **Species by mating with** *Escherichia coli*. *Science*. 1959, Sept. 4, v. 130, 566–7. [13 refs.]

MATSUI, S. **Antigenic Changes in** *Shigella flexneri* **Group by Bacteriophage.** *Japanese J. Microbiol.* 1958, Apr., v. 2, No. 2, 153–8. [16 refs.]

When *Shigella flexneri* 1a was grown in broth containing a sterile filtrate from repeatedly frozen and thawed cultures of *Sh. flexneri* 4 c plate cultures yielded a mixture of colonies some of which had the antigenic structure of *Sh. flexneri* 4. Similarly a strain of *Sh. flexneri* 3b grown in broth containing the same sterile filtrate, obtained from *Sh. flexneri* 4, also resulted in the isolation of a few colonies possessing type IV antigen only, other colonies appeared to be a mixture of types III and IV with a loss of the group factor 4. Cross absorption tests with the parent strains and the variant indicated a true change of type.

With the agar layer technique the bacterial filtrate was shown to lose its test strain; a plaque count of $4{\cdot}5 \times 10^4$ was obtained to *Sh. flexneri* 1a and $4{\cdot}0 \times 10^4$ to 3b. It was considered that the antigen changing factor was the released temperate phage possessed by the strain of *Sh. flexneri* 4c. When the biological characters of the variants were studied they were found to be identical with those of the parent strain. *H. J. Bensted*

WEINBACH, R Über ein merkwürdiges Verhalten von Kaninchen-Sh.-sonnei R-Immunsera in der indirekten Haemagglutination. [**An Unusual Behaviour of Rabbit *Shigella sonnei* R Immune Sera in the Indirect Haemagglutination Test.**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Mar., v. 117, No. 3, 244–55. [11 refs.]

The author has made further investigations of the indirect haemagglutination test with *Shigella sonnei* R antiserum, which is carried out by sensitizing formolized sheep red cells with an extract of the organisms and then incubating the red cell suspension with serial dilutions of the antiserum for 2 hours at 37°C. In an example quoted haemagglutination occurred to a titre of 512. When an attempt was made to carry out an inhibition titration by mixing constant volumes of antiserum with serial dilutions of antigen and adding the sensitized red cells after incubation for 30 minutes at 37°C., it was found that haemagglutination occurred in the tubes containing higher concentrations of antigen, and partial haemagglutination could still be observed with an antigen dilution of 1:2048. The agglutination was in most cases stronger than that observed in a control tube not containing antigen. Various possible explanations of the effect are discussed. *D. J. Bauer*

KLECKOVÁ ALDOVÁ, E. & JELÍNEK, J., with the technical assistance of E. ZELENÉ. K některým aktuálním otázkám epidemiologie, léčby a prevence bacilární dysenterie. I. Sulfonamidorezistence shigel. [**Some Actual Problems of Epidemiology, Therapy, and Prophylaxis of Bacterial Dysentery. Part I. The Resistance of Shigellae to Sulphonamide**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 3, 157–67, 2 graphs & 2 figs. [34 refs.]. English summary.

An investigation has been made of the resistance to sulphonamides of 1,935 strains of 4 species of *Shigella* isolated during epidemics and from sporadic cases of dysentery in Czechoslovakia. Resistance was observed in 111 of 1,426 (7·8%) strains of *Sh. sonnei* and in 73 of 462 (15·8%) strains of *Sh. flexneri*; a high proportion of resistant strains (36·6% of 71 strains) was observed in the serotype *Sh. flexneri* 2a. *D. J. Bauer*

OLARTE, J. & DE LA TORRE, J. A. **Resistance of *Shigella flexneri* to Tetracyclines, Chloramphenicol and Streptomycin. A Study of 131 Freshly Isolated Strains.** *Amer. J. Trop. Med. & Hyg.* 1959, May, v. 8, No. 3, 324–6.

Of 31 strains of *Shigella flexneri* isolated in Mexico City in 1953, none was resistant to tetracycline. A further 100 strains were isolated during the years 1955–7, and the percentage frequencies of resistance to tetracycline in these 3 years were 19, 34 and 39. This was a period during which the tetracyclines came into extensive use. Resistance to chloramphenicol also made its appearance during this time, but the percentage of resistant strains never exceeded 8. An opposite change occurred in resistance to streptomycin, the frequency of which fell from 74 to 39%: this corresponded to diminished use. There was some relationship between serological type and resistance to the 2 latter antibiotics, but not to tetracycline. *L. P. Garrod*

WORTHEN, L. R., CZARNECKI, R. B., BENNETT, E. & FULLER, J. E. **Studies on the Role of Glycosides in the Identification and Differentiation of Enteric Bacteria.** *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 384–8.

This paper is mainly concerned with an assessment of the differentiating value of salicin, arbutin, aesculin and methyl-α-D-glucoside in identifying members of the Enterobacteriaceae. The most important results of the present study appear to be the confirmation of the value of methyl-α-D-glucoside in differentiating *Escherichia coli* from *Aerobacter aerogenes* and the fact that all cultures of *Shigella sonnei* examined were found to be capable of producing acid when arbutin was present in the medium. Of the salmonella strains examined *Salm. florida* alone produced acid and gas from methyl-α-D-glucoside; all other salmonella species examined failed to ferment this glycoside. *H. J. Bensted*

HAMON, Y., with the technical collaboration of G. BRAULT. Recherche et identification de la propriété colicinogène parmi les différents lysotypes d'*Escherichia coli* pathogènes pour le nourrison. Intérêt épidémiologique de cette étude. [**Demonstration and Identification of Colicinogenic Property in the Different *E. coli* Phage-Types, Pathogenic for Infants. Epidemiological Significance of this Study**] *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 614–29. [12 refs.]

The colicinogenic property of *E. coli* strains associated with gastro-enteritis and belonging to several different phage types was investigated by an examination of the following:—424 strains of 0111:B4, 275 strains of 055:B5 and 98 strains of 026:B6. These 797 strains were selected from a collection in such a way as to represent a wide variety of phage types. Also investigated were 59 strains from outbreaks of gastro-enteritis (51 of 0119, 7 of 0127 and 1 of 0136). Finally, 141 cultures of *E. coli* from 40 epidemic centres in Germany (Keil and Wernigerode-Harz) were used to evaluate the epidemiological uses of colicine identification.

It was found that colicinogenic activity is best preserved by storing the culture at 40°C. in Dorset's egg medium, and that the strains examined produced the following colicines—I, E1, E2, B, G, E1 + I, E2 + I, G + I, E + B—or else appeared to possess no colicinogenic properties. Examination of the epidemic strains showed that each epidemic produces organisms with similar colicinogenic properties. It is concluded that both the phage type and colicinogenic state of strains of *E. coli* occurring in gastro-enteritis should be investigated in order to produce more precise results. [See also FREDERICQ *et al*, this *Bulletin*, 1957, v. 32, 363.] *John S. Stevenson*

DOUDNEY, C. O. & HAAS, F. L. **Effect of Purine and Pyrimidine Analogues on Reversion of a Tryptophan-requiring Strain of *Escherichia coli*.** [**Correspondence.**] *Nature.* 1959, July 11, v. 184, 114–15.

BILLEN, D. **Influence of Unbalanced Growth on Subsequent X-Ray-Induced Inhibition of Deoxyribonucleic Acid Synthesis in** *Escherichia coli* 15 *T. Nature.* 1959, July 18, v. 184, 174–6, 2 figs. [14 refs.]

LASER, H. & THORNLEY, Margaret J. **Stimulation by X-Radiation of Enzyme Induction and Growth in** *Escherichia coli. Proc. Roy. Soc.* Ser. B. 1959, Sept. 1, v. 150, No 941, 539–53, 10 figs. [13 refs.]

BOLCATO, V. **Glyoxylate Intermediate of the Direct Oxidation of Acetate and Glycolate by** *E. coli. Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 2, 179–82. [10 refs.]

RICKENBERG, H. V. **The Effect of Metal Ions and Proteins on the Stability of the β-Galactosidase of** *Escherichia coli. Biochim et Biophys. Acta.* 1959, Sept., v. 35, No. 1, 122–9, 2 figs. [12 refs.]

COCITO, C. & VANDERMEULEN-COCITO, J. **Properties of a Colicine, selectively inhibiting the Growth of** *E. coli* **B and favoring Multiplication of Mutants Resistant to Phage T3, in Static and Continuous Cultures.** *Giorn. di Microbiol.* Naples. 1958, July–Dec., v. 6, Nos. 1, 2 & 3, 146–79, 6 figs. (2 on pl.). [33 refs.]

GLASKY, A. J. & RAFELSON, M. E., Jr. **The Utilization of Acetate-C^{14} by** *Escherichia coli* **grown on Acetate as the Sole Carbon Source.** *J. Biol. Chem.* 1959, Aug., v. 234, No. 8, 2118–22. [32 refs.]

HANAWALT, P. **Use of Phosphorus-32 in Microassay for Nucleic Acid Synthesis in** *Escherichia coli. Science.* 1959, Aug. 14, v. 130, 386–7. [10 refs.]

YANOFSKY, C. & LENNOX, E. S. **Transduction and Recombination Study of Linkage Relationships among the Genes controlling Tryptophan Synthesis in** *Escherichia coli. Virology.* New York. 1959, Aug., v. 8, No. 4, 425–47, 2 figs. [18 refs.]

MCCARTHY, B. J. & HINSHELWOOD, C. **The Phosphatase Activity of** *Bacterium lactis aerogenes. Proc. Roy. Soc.* Ser. B, 1959, Sept. 1, v. 150, No. 941, 474–85, 6 figs. [27 refs.]

"In the early stages of a growth cycle of *Bact. lactis aerogenes* in a glucose-ammonium sulphate medium the phosphatase activity of the cells rises to high levels from which it later declines, as though by progressive dilution with less active material. The decline is not prevented by maintenance of a constant pH, nor by periodic dilution with fresh medium so as to keep the cell count in unit volume near a steady mean. The pattern of variation depends on the medium: for example, amino acid additions lower the maximum, replacement of glucose by acetate prevents the decline, absence of molecular oxygen leads to a low activity throughout."

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LARK, Cynthia & LARK, K. G. **The Effects of D-Amino Acids on** *Alcaligenes fecalis. Canadian J. Microbiol.* Ottawa. 1959, Aug., v. 5, No. 4, 369–79, 3 figs. [18 refs.]

LARK, K. G. **Isotopic Competition between D- and L-Methionine in** *Alcaligenes fecalis. Canadian J. Microbiol.* Ottawa. 1959, Aug., v. 5, No. 4, 381–94, 3 figs. [12 refs.]

BACHRACH, U. & WORMSER, M. **Practical Laboratory Tests for the Identification of** *Proteus* **Strains.** *J. Clin. Path.* 1959, July, v. 12, No. 4, 376–7. [10 refs.]

The rapid diagnosis of *Proteus* species is often made by testing for urease. This paper describes a method in which filter-paper impregnated with urea and indicator is added to a concentrated suspension of bacterial cells. A urease-producing organism makes the paper turn pink, and the pink colour persists. A transient pink colour develops when growths from alkaline media are used to make the suspensions, but when these organisms are not urease-producing the pink colour soon fades.

To test for volatile amines, broth cultures are capped with filter paper soaked in 2:4 dinitro-fluoro-benzene reagent and the tubes put in a boiling water bath for 15 minutes. A yellow colour indicates volatile amines. This test was positive only with *Proteus* spp., the Providence group (isoamyl and isobutyl amines) and *Streptococcus faecalis* (phenylethylamine amine).

S. T. Cowan

MARTINEZ, R. J., WOLFE, J. B. & NAKADA, H. I. **Degradation of Chondroitin Sulfate by** *Proteus vulgaris. J. Bacteriology.* 1959, Aug., v. 78, No. 2, 217–24, 5 figs. [25 refs.]

KLEINMAIER, H. & QUINCKE, G. Über das Vorkommen der Serotypen von *Pseudomonas aeruginosa.* [**Incidence of** *Pseudomonas pyocyanea* **Serotypes**] *Arch. f. Hyg. u. Bakt.* 1959, Feb., v. 143, No. 2, 125–34, 1 graph. [12 refs.]

The authors present an analysis of the incidence of a number of commonly occurring microbial forms in a variety of specimens, about 5,000 in all, sent into the laboratory.

From urinary specimens, *Escherichia coli* was most common, accounting for 26%, *Proteus* next with 13%, then *Staphylococcus aureus* and *Aerobacter*, both with 5% and *Pseudomonas pyocyanea* 3%. The highest percentage of *Pseudomonas* infection (16·6) occurred in ear discharges.

Classifying 500 strains of *Ps. pyocyanea* by methods previously used by the senior author [this *Bulletin*, 1959, v. 34, 171] and by HABS [*ibid.*, 1958, v. 33, 989], they were able to separate them into 6 larger groups, 6 smaller groups and 82 ungrouped strains, of which 27 gave unstable suspensions in salt solution.

J. W. McLeod

HARTMANN, Dora. Beobachtungen bei der bakteriologischen Diphtherie-Diagnostik 1957/58 in West-Berlin. [**Bacteriological Examinations in Diphtheria Cases in Berlin in 1957 and 1958**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 3/4, 228–35, 1 fig. [14 refs.]

The laboratory concerned serves the North part of West Berlin. As in other areas of Europe a steady recession of cases of diphtheria had occurred up till 1954. From 1955 onwards, however, the disease has reappeared with a rather peculiar distribution both in respect of the cultural variants of *Corynebacterium diphtheriae* and the incidence of significant clinical illnesses.

Well defined *gravis, intermedius* and *mitis* strains which have retained their characters through many subcultures have been responsible for this recent diphtheria. The frank clinical cases have occurred with few exceptions in the younger children of the refugee camps and have been associated with *intermedius* and *gravis* strains whereas the *mitis* strains which have almost invariably been non-toxigenic have been recovered from carriers in all age-groups in the indigenous population of Berlin.

Among the clinical cases 3 deaths, 1 severely toxic diphtheria and 9 complicated cases (myocarditis, polyneuritis or nephritis) have been observed; these have all been *gravis* infections. The *gravis* strains appear to be better toxin producers than the *intermedius* in agar diffusion plates but this is probably explained by heavier growth of the former. In animal tests, the two varieties appear equally toxic.

In the course of 1½ years the following have been isolated:

182 toxin-forming *gravis*
101 „ „ *intermedius*
222 non-toxin-forming *mitis*.

The only other interesting feature is that the *intermedius* strains have appeared to play a special role in nasal diphtheria.

There was a very definite epidemic incidence of *gravis* for a short period about mid winter 1957/58.

J. W. McLeod

LEVINA, L. A. **The Influence of Diphtheria Toxin upon the Local Inflammatory Reaction—I. The Specific Intensification by Diphtheria Toxin of the Inflammatory Reaction in the Skin of Guinea-Pigs caused by Live Atoxigenic Strains of** *Corynebacterium diphtheriae*. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 9, 1384–9. [16 refs.] [Translated from Russian.]

An enhanced reaction was obtained when an injection of live non-toxigenic diphtheria bacilli was associated with a small dose of toxin (filtrate of PW8 strain). This reaction was specific to the extent that small doses of staphylococcal and streptococcal culture filtrates capable of producing slight reactions did not enhance the reaction to the non-toxigenic cells of *C. diphtheriae*.

J. W. McLeod

[In the English version of this paper the fifth word from the end of the title reads "toxigenic". For the purposes of this abstract that word has been altered to "atoxigenic", which is correct according to the original Russian title and which is used throughout the English text. The general use of the term "non-toxigenic" in the literature would avoid errors of this kind.—*Ed.*]

LONG, D. A. **Immune and Allergic Reactions to Diphtheria Toxin and Toxoid in Guinea-Pigs.** *J. Hygiene.* 1959, June, v. 57, No. 2, 216–26, 9 figs. [16 refs.]

An elaborate study of the reaction of guineapigs to diphtheria toxin and toxoid is presented with a view to exploring the hypothesis that the reaction is due to an early response of an Arthus-like type and a later or tuberculin-like reaction. It is supposed that the former is due to circulating precipitating antibody and the latter to cellular immunity.

Actually, the first could be transferred passively with the serum of an immunized guineapig but attempts to demonstrate a transfer of the latter with cellular exudate from the peritoneum of an immunized guineapig was less successful. A surprising amount of immune antibody was, however, transferred with the cells, mainly lymphocytes, and an Arthus-like reaction—increased skin oedema in the injected area—appeared in guineapigs passively immunized with such cellular exudates and tested with toxoid.

J. W. McLeod

LONG, D. A. **The Fate of ^{131}I-Labelled Diphtheria Toxin and Toxoid in the Skin of Immune and Allergic Guinea-Pigs.** *J. Hygiene.* 1959, June, v. 57, No. 2, 227–34, 8 figs.

Highly purified toxin and toxoid were labelled with radioactive ^{131}I.

When such material is injected into actively immunized animals the radioactive material disperses slowly from the site of injection whereas in non-immunized animals it is dispersed rapidly.

Assuming that the radioactive iodine remains attached to the toxoid or toxin injected, it is concluded that a localized tissue reaction is responsible for the retention of the toxoid in the area of injection and that this reaction may be similar in character to the delayed effect responsible for the tuberculin reaction. This capacity to localize toxoid cannot be transferred to an animal passively by injection of the serum of an immunized animal.

J. W. McLeod

WEISS, D. W. **The Effects of Mechanical Agitation on the Growth of the H37Ra Strain of** *M. tuberculosis*. *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 813–15.

By incubating cultures of H37Ra in Dubos medium on a Brunswick gyratory shaker at 80 r.p.m. the yield of bacilli was increased 9-fold as compared with that from static incubation, and this proportional increase was the same whether Tween 80 was present or not. The growth-enhancing effect of the agitation was greatest with large inocula or when the cultures were incubated for 7 days before being shaken; with small inocula the shaking retarded growth, and if no Tween was present

the bacilli grew in discrete pellets with many of the bacilli non-acid-fast.

The enhancing effect was shown to depend on the constituents of the medium, *e.g.* raising the concentration of the Tween to 1·0%, the sodium acetate to 0·3% or the sodium lactate to 0·3% decreased the enhancing effect, whereas increasing the glycerol to 1–6% increased it. Similar observations were made with the BCG-Phipps and R1Rv strains.

Deep cultures with aeration also produced increased yields, especially with the BCG-Tice strain, which grew very sparsely in static cultures.

These observations are of especial value for the production of non-viable vaccines. [See also this *Bulletin*, 1959, v. 34, 484.] *S. R. M. Bushby*

Diena, B. B., Eidus, L. & Greenberg, L. **A New Method of counting the Viable Organisms in BCG Vaccine.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 816–17.

In this method dilutions of the BCG vaccine are made in buffered Sauton medium containing 5% human serum, and after being shaken for 2½ hours at 200–225 oscillations per minute, 1 ml. is poured over the surface of 25–30 ml. of Tarshis blood medium in a 250 ml. Erlenmayer flask. During the first 2 weeks' incubation all movement is avoided and during this time the fluid evaporates. The colonies become apparent by the 12th day, but in 21 days they are distinct, circular, raised and light brown in colour.

The method was compared with 6 other methods and the advantages claimed are that as the medium is never completely dry, better colonial appearances are obtained, the results are more uniform and available earlier, the colonies are easier to count, and the buffered medium reduces bacterial contamination.

The procedure is considered to have interesting potentialities in diagnostic work with mycobacteria.

S. R. M. Bushby

Konno, K. & Sbarra, A. J. **Differentiation of Human Tubercle Bacilli from Atypical Acid-Fast Bacilli. III. Modification of the Niacin Test, using Tween-Albumin Liquid Medium.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 810–12. [14 refs.]

Human tubercle bacilli have been shown to produce more niacin than the bovine or the avian strains [this *Bulletin*, 1958, v. 33, 983]. This is confirmed in the present paper where it is also shown that a positive test can be obtained in 10 days with cultures in Dubos medium as compared with 1 month with cultures on solid media, the aniline mixture and the cyanogen bromide being added directly to 3 ml. of culture. Quantitative estimations showed that 10 μgm. of niacin was produced from the equivalent of 1 mgm. of dried bacilli from the fluid medium as compared with 0·15 μgm. from the same weight of bacilli from the solid medium.

[In a recent paper [*ibid.*, 1959, v. 34, 1168] it was shown that the use of the primary cultures on solid media could be made very sensitive if the niacin were extracted from the media with 0·5–1·0 ml. water.]

S. R. M. Bushby

Yamamura, Yoshihire, Tani, J., Terai, T. & Yamamura, Yuichi. **Studies on the Virulence of Tubercle Bacilli using P^{32}-Labelled Bacilli. I. The Comparison of Elimination *in Vivo* of P^{32} derived from Heat-Killed Virulent and Avirulent Tubercle Bacilli.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 738–45, 8 figs. [15 refs.]

There is experimental evidence that indicates that virulent tubercle bacilli have a toxic substance which makes their phagocytosis, digestion and elimination by the host slower than that of the avirulent strains. In the present paper the authors present evidence that shows that the toxic lipid fraction plays an important role in retarding the elimination of the virulent strain.

In these experiments the bacilli were grown in Sauton medium containing 10–20 mC of $Na_2H^{32}PO_4$ per ml., and the radioactive bacilli, after being killed by heat, were injected intravenously into mice. The rate of elimination of the bacilli was followed by measuring the radioactivity of homogenates of the whole body and of the liver of mice killed at intervals up to 25 days after inoculation. The strains of bacilli examined were H37Rv, a virulent bovine strain, H37Ra, BCG, 2 avian strains and Mycobacterium 607. Killed bacilli were used to avoid loss of radioactivity through metabolism of the bacilli.

The rates of elimination of the avian and avirulent strains were rapid as compared with those of the virulent strains and of BCG; that of Myco. 607 was intermediate. However, although when the bacilli were extracted by Anderson's method with alcohol and ether the rates were only slightly altered, when this extraction was followed by a further extraction with chloroform the rates of elimination of all the strains became identical. The calculated half-diminution time of the ^{32}P of the virulent strains and BCG was 3–5 times longer than that of the avirulent or the strains extracted with chloroform.

S. R. M. Bushby

Tysarowski, W. & Kwiek, S. **Studies of the Catalase Activity of Mycobacterium Tuberculosis Strain H37Rv.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 257–8, 2 figs.

"The relationship between catalase activity and pH is illustrated in figure 2. The optimal of pH for the strain of H37Rv is about 7.

"The present findings indicate that the relations between the catalase activity of the strain *M. tuberculosis* H37Rv and temperature, as well as pH, are similar to those of other known catalases, provided a suitable method of investigation is applied."

Dâmboviceanu, Aristia, Vainer, Henriette & Ionescu-Mihăiești, C. Contenu en amino-acides des tuberculoprotéines elaborées par différents types de mycobactéries pathogènes et saprophytes. [**The Amino-Acid Contents of Tuberculoproteins formed by Various Types of Pathogenic and Saprophytic Mycobacteria**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Mar., v. 18, No. 1, 1–8, 1 fig.

MAUER, H. & KNOTHE, H. Über eine durch *Bacillus cereus* bei *Mycobacterium tuberculosis* bewirkte Oxydation. (1. Mitteilung.) *Zent. f. Bakt.* II. Abt. 1959, Aug. 25, v. 112, Nos. 16/20, 544–52, 7 figs. [12 refs.] Untersuchungen über die Spezifität eines bei *Mycobacterium tuberculosis* wirksamen Oxydationsfermentes. (2. Mitteilung.) *Ibid.*, 553–60, 8 figs. Allgemeine Eigenschaften des Oxydationsfermentes von *Bacillus cereus*. (3. Mitteilung.) *Ibid.*, 561–6, 6 figs. Beiträge zur Aufklärung der Wirkungsweise der bei *Mycobacterium tuberculosis* beschriebenen durch *Bacillus cereus* bewirkten Oxydation. (4. Mitteilung.) [**I. An Oxidation Process Active in** *Mycobacterium tuberculosis* **Brought About by** *Bacillus cereus*. **II. Specificity of an Oxidation Enzyme Active in** *Myco. tuberculosis*. **III. General Properties of the Oxidation Enzyme of** *B. cereus*. **IV. Clarification of the Activity of the Oxidation Process Brought About by** *B. cereus* **in** *Myco. tuberculosis*] *Ibid.*, 567–76, 7 figs.

GOLDMAN, D. S. & GELBARD, A. **Enzyme Systems in the Mycobacteria. VIII. The Fatty Acid Oxidizing System.** *Arch. Biochemistry.* 1959, Aug., v. 83, No. 2, 360–70, 5 figs. [25 refs.].

NAYLOR, R. F. **A Study of the Action of Sulfones on the Metabolism of Mycobacteria.** *Internat. J. Leprosy.* Wash. 1958, Oct.–Dec., v. 26, No. 4, Pt. 1, 313–17.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1245.]

BINFORD, C. H. **Histiocytic Granulomatous Mycobacterial Lesions produced in the Golden Hamster (*Cricetus auratus*) inoculated with Human Leprosy. Negative Results in Ten Experiments using other Animals.** *Internat. J. Leprosy.* Wash. 1958, Oct.–Dec., v. 26, No. 4, Pt. 1, 318–24.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1247.]

KAPRAL, F. A. & SHAYEGANI, M. G. **Intracellular Survival of Staphylococci.** *J. Exper. Med.* 1959, July 1, v. 110, No 1, 123–38, 10 figs.

A tissue culture technique was used to study the intracellular survival of staphylococci in rabbit, human and rat leucocytes.

Rabbit monocytes obtained by peritoneal washing after injection of mineral oil were mixed with coagulase positive staphylococci and placed in Porter flasks containing coverslips in a medium with and without streptomycin. Coverslips were removed at intervals, stained and the distribution of intracellular staphylococci was determined. Samples from streptomycin-free flasks showed a rapid increase in the number of cells containing many organisms and rapid destruction of the leucocytes. Samples from flasks containing sufficient streptomycin to prevent extracellular growth showed no change in the relative frequency of intracellular cocci but it was not possible to determine if the organisms were living or dead.

A plastic tissue culture chamber which is fully described was used in subsequent experiments. It has grooves into which fit a series of coverslips. The chamber was filled with monocyte-staphylococci mixture incubated to allow phagocytosis and adherence of the cells to the coverslips. The fluid was then removed from the chamber, which after washing was refilled with medium with or without streptomycin, and reincubated. At each sampling 2 coverslips and 0·5 ml. of medium was removed. The medium sample was serially diluted and plated for extracellular organisms. One coverslip was stained and the total number of cells calculated. The other coverslip was crushed in saponin with ballotini and serial dilutions made and plated to determine the total number of intracellular staphylococci. The average number of cocci per cell could then be calculated.

If no streptomycin was present the average number of intracellular cocci began to increase when the concentration of organisms in the medium was 10^5–10^6 ml. Many cells contained 200–300 organisms after about 3 hours. If streptomycin was present or if the number of extracellular organisms was kept low by frequent washing and phagocytosis was prevented, the average number of viable cocci remained constant. A coagulase-negative strain however was progressively destroyed with an intracellular half-life of about 2–5 hours.

Intracellular cocci were also seen to survive but not multiply when rabbit neutrophils and human leucocytes replaced rabbit monocytes but *Staph. aureus* and *Staph. albus* were both progressively destroyed by rat monocytes when streptomycin was used to prevent extracellular growth. *M. Patricia Jevons*

HAUGHTON, G. & DUTHIE, E. S. **Activation of Staphylococcal-Free Coagulase by Purified Human Prothrombin.** [Correspondence.] *Nature.* 1959, July 11, v. 184, 116. [10 refs.]

PIERCE, W. A., Jr. **Agar Diffusion Studies of Group A Streptococcal Antigens.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 726–32. [36 refs.]

The antigens produced by 3 strains of *Streptococcus pyogenes* (types 14, 12 and 36) were studied by means of the double diffusion agar tube technique. Antigen preparations obtained from each strain included concentrated broth culture supernatant, disrupted cell extract, hot acid extract of an 18-hour culture and a crude preparation of M protein derived from the hot acid extract by ethanol precipitation. Antisera were prepared by using heat-killed vaccines of the 3 strains. The crude M protein fractions were antigenically complex showing as many as 10 different precipitate zones with homologous antiserum and containing multiple non-specific components cross reacting with heterologous antisera. The antigenic activity of all these components was removed by digestion with trypsin.

H. Gooder

PACE, M. Geraldine & PAPPENHEIMER, A. M., Jr. **An Immunochemical Study of Streptococcal Diphosphopyridine Nucleotidase.** *J. Immunology.* 1959, July, v. 83, No. 1, 83–6, 1 fig. [11 refs.]

Streptococcal diphosphopyridine nucleotidase (DPNase) (*J. Exper. Med.*, 1957, v. 106, 27) was

concentrated and purified by absorption on alumina gel, elution at alkaline *p*H followed by salt fractionation and continuous flow curtain electrophoresis. The highest specific activity obtained was 25,000 units DPNase per μgm. trichloroacetic acid precipitable nitrogen. Immunochemical studies of the DPNase-anti-DPNase system were carried out with the purified enzyme and globulin fractions prepared from rabbit antisera. Similar quantitative behaviour was found with γ globulin prepared against "free" DPNase and against a DPNase-anti-DPNase complex obtained as a specific precipitate in the region of antibody excess.

H. Gooder

HALL, R. H. & GALE, G. O. **New Observations on Pneumococcal Transformations** *in vivo*. *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 487–91. [11 refs.]

Mice were injected subcutaneously with living non-virulent pneumococci mixed with a heat-killed vaccine of a virulent strain; *in vivo* transformation of the non-virulent strain resulted in death of the animals. The heat-killed vaccine was successfully replaced by a purified preparation of the transforming principle from it. This transforming principle was inactivated by treatment with dodecyl sulphate or chloroform. The living cocci were transformed even if they were injected, intraperitoneally, 24 hours after the subcutaneous injection of the transforming principle. Streptomycin resistance was also produced by *in vivo* transformation.

R. E. O. Williams

MEYER, Margaret E. & CAMERON, H. S. **Comparative Metabolism of Species and Types of Organisms within the Genus** *Brucella*. *J. Bacteriology*. 1959, July, v. 78, No. 1, 130–36. [26 refs.]

Strains were classified by dye sensitivity and H_2S production into 3 types of *Br. abortus*, one of *Br. melitensis*, 3 of *Br. suis*, and 2 strains were regarded as a new species, *Br. neotomae*. Resting cell suspensions of the 27 strains were added to various amino acids and carbohydrates, and the oxygen uptakes were measured.

A table shows that the metabolic patterns of *Br. abortus* III and *Br. melitensis* I were similar; those of *Br. suis* II and *Br. neotomae* were each distinctive, but those of *Br. abortus* I, II and *Br. suis* I and III were similar. [The authors are more optimistic and claim that all types are distinctive.] *S. T. Cowan*

GLENCHUR, H., HALL, W. H. & ZINNEMAN, H. H. **Blocking Antibodies in Rabbits infected with** *Brucella melitensis*. *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 422–5, 2 figs.

"Six rabbits were infected intravenously with a single massive dose of *Br. melitensis*. Three were treated by subcutaneous administration of streptomycin and tetracycline for 2 weeks and 3 were left untreated. The untreated rabbits developed a markedly increased gamma globulin content in their serum, which was not appreciably changed by absorption with killed whole *Br. abortus* cells. In addition, the blocking phenomenon was demonstrated in low titres in serum of these rabbits by 29th day of infection. Antibiotic therapy was effective in preventing the rise of gamma globulins and of blocking antibody through the 59th day."

KAMAL, A. M. **Studies on the Cultivation of Brucella Abortus in the developing Chick Embryo. I. Qualitative and Quantitative Studies on the S-Form.** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 7/8, 544–58, 2 figs. [24 refs.]

Using the same smooth strain of *Brucella abortus* throughout, the author determined 5 issues as below.

(1) Studying the distribution of the organisms after their inoculation into the yolk sac, allantoic cavity, amniotic cavity, the embryo and on the chorio-allantois, he found that after all the above routes of injection, *Br. abortus* was recovered from all internal organs of the embryo (with the possible exception of the brain after embryonal inoculation), the blood, the extra-embryonic membranes and fluids of the egg. The number of organisms inoculated was 2 million, except into the amniotic cavity and the embryo itself where it was 1 million.

(2) In 6-day-old embryos, inoculated into the yolk sac with only 4 organisms, infection and death ensued in 6 of 6 experiments between the 6th and 8th days after injection. Of 6 embryos, each infected with an estimated 2 organisms, 2 died before hatching, the remaining 4 hatched normally and at post mortem there was no evidence of infection nor could *Br. abortus* be recovered. Agglutination tests on the sera of these 4 chicks were however positive (1/50) suggesting that infection had been overcome. It appeared from these results that the resistance of embryonic tissues to infection was of a very low order.

(3) Embryos aged from 4 to 14 days old when injected *via* the yolk sac with 2 million *Br. abortus* were subject to disease. The older the embryo when inoculated the longer the time between inoculation and death: all those injected on or before the 11th day of age died before hatching, whereas all those injected on the 14th day hatched, but only to die before the end of a week. *Br. abortus* was recovered from the organs of the latter and serum agglutination titres between 1/300 and 1/600 were found.

(4) He ascertained the growth curves for *Br. abortus* (a) in the embryo proper and (b) in the whole egg after injecting 10,000 organisms into the yolk sacs of 5-day-old embryos. Eggs were taken after 12 and 24 hours and thereafter daily up to 12 days and (a) the embryo or (b) the whole egg was homogenized for the purpose of making viable counts. For the embryo proper a classical growth curve was obtained. The end of the logarithmic phase (4 days) coincided with death of the embryo. It was therefore concluded that viability of the embryo was necessary for the multiplication of *Brucella* within it.

The curve (b) for the whole egg showed almost no lag phase, and a gradual flattening out of the logarithmic phase after 2 days until at 5 days a stationary period ensued. Since embryos were dead on the 4th day it appeared that some bacterial multiplication took place for 1 day after death.

(5) After the yolk-sac injection of 100,000 *Br. abortus* into 9-day embryos, the number of organisms per unit weight of embryonic tissue in descending numerical order was blood, heart, spleen, liver, kidney, allantoic fluid, chorio-allantoic membrane, yolk sac, amnion membrane, yolk and amniotic fluid.

J. G. P. Hutchison

LOGAN, J. E., GRIFFITHS, B. W. & MASON, M. A. **Specificity of the Clearance Phenomenon in the Lungs of Pertussis-Immunized Mice following Intratracheal Administration of Radioiodinated Pertussis Vaccine.** *Canadian J. Microbiol.* Ottawa. 1959, Aug., v. 5, No. 4, 405–13 [22 refs.]

"In mice which were immunized with various immunizing agents 6 and 20 days prior to challenge, it was found that stimulation of lung clearance of intratracheally administered radioiodinated pertussis vaccine was observed chiefly in those mice which had received vaccine prepared from any of the three members of the genus *Bordetella*. The most marked effect occurred in the pertussis-immunized animals. In pertussis-immunized mice which were challenged intratracheally with heterologous radioiodinated antigens, the most significant increases in clearance were obtained in those animals receiving labeled *bordetella* vaccines. When mice immunized with the various antigens were challenged by their labeled homologous antigens, again the most significant clearance stimulations occurred in the mice immunized and challenged with the *Bordetella* preparations. Clearance studies with mice immunized and/or challenged with a vaccine prepared from phase IV pertussis organisms would support a view that somatic antigens may stimulate lung clearance in mice immunized 6 days prior to challenge whereas the surface antigens may provoke a slower-developing and longer-lasting immunity that is responsible for the faster clearance observed 20 days after immunization."

KUWAJIMA, Y, MATSUI, T., NAKA, K. & KISHIGAMI, M. **Histo-Pathological Changes in Lungs of Guinea Pigs inoculated with the Sonic Extract of** *Bordetella pertussis*. *Osaka City Med. J.* 1959, v. 5, No. 1, 81–6, 6 figs.

"The occurrence of interalveolitis in guinea pigs was observed following the inoculation of the Phase I extract and following the injection of the Phase III or R type extract. The Phase I extract heated at 100°C was also able to induce interalveolitis. The occurrence could not be prevented by anti-Phase I serum."

CHIBRIKOVA, E. V., KUZNETSOVA, V. I., BAZUNOVA, L. P. & DUDKOVA, V. K. **The Accelerated Detection of** *Vibrio comma* **in Water and in Washings from Objects in the Surroundings by means of Fluorescence Microscopy.** *J. Microbiol., Epidemiol & Immunobiol.* London. 1958, v. 29, No. 10, 1591–5. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 59, 1233.]

MEISEL, H. & RYMKIEWICZ, Danuta. Antygeny zarodnikowe w klasyfikacji proteolitycznych *Clostridia*. **[Spore Antigens in the Classification of Proteolytic** *Clostridia***]** *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 1, 1–12. English summary.

The authors have investigated the applicability of spore agglutination by specific antisera in the classification of various species of the genus *Clostridium*. The investigations were carried out with 30 strains belonging to the species *Cl. sporogenes*, *Cl. histolyticum*, *Cl. botulinum* types A and B, *Cl. sordelli*, *Cl. bifermentans* and *Cl. tetani*. Rabbits were immunized by the intravenous injection of suspensions of spores freed by enzyme treatment from remnants of bacterial cells, and the antisera thus obtained were used in conventional agglutination tests in which the same spore suspensions were used as antigens. A slight degree of cross-reaction to a titre of 320 was observed between *Cl. sporogenes* and *Cl. histolyticum*, but no cross-reactions occurred with the remaining species, which could thus be distinguished on the basis of their major antigens. Minor antigens could also be detected, and the antigenic compositions of the strains examined are presented in a table.

D. J. Bauer

MILLER, Pauline A, EATON, M. D. & GRAY, C. T. **Formation of Tetanus Toxin within the Bacterial Cell.** *J. Bacteriology*. 1959, June, v. 77, No 6, 733–40, 3 figs. [11 refs.]

The authors have made an analysis of the distribution of tetanus toxin between the supernatant fluid and the bacterial cell. They find that the toxin content of cells which have been carefully washed free from the culture fluid and any toxin which it contains, can be accurately estimated in experimental work on mice.

The dose which is sufficient to produce definite tetanic symptoms in the animals without killing them is described as the toxic dose and an amount 10 times greater than this is found to kill mice with great regularity whereas an amount 10 times less fails to produce symptoms in the experimental animal.

Experimental evidence is submitted to show that there is no difference between the effect of such cells when injected with or without amounts of penicillin adequate to suppress any growth in the tissues, and it is therefore assumed that such growth does not lead to toxin formation after the bacilli have been introduced into the animal's body and give rise to misleading results due to liberation of fresh toxin after the bacilli have been injected.

With such preparations in the examination of cultures in a variety of media, it is claimed that more accurate indications of their capacity for stimulating toxin production can be obtained than with filtrates of cultures, since the toxin present in such is determined by 2 factors, the amount of toxin produced and the extent to which it has been liberated in the disintegration of the bacterial bodies.

In experimental work based on such observations, the conclusion is reached that toxin production, which is good in the pancreatic digest medium of MUELLER and MILLER [this *Bulletin*, 1954, v. 29, 880] and also in

their defined medium containing histidine peptide, fails if the latter is omitted from the second medium [*ibid.*, 1956, v. 31, 457]. *J. W. McLeod*

KATITCH, R. V. Sur la valeur hémothérapeutique et immunogène de la séro-anatoxithérapie du tétanos. [**Immunological Value of Antitoxin-Toxoid Treatment of Tetanus**] *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No 3, 133–44. [21 refs.]

A number of observations are recorded which bear on the effect of anatoxin (formol toxoid) when injected together with small lethal doses of toxin. The observation that a number of animals survive when such injections are made is confirmed and the explanation of this result is found to lie in the effect of the excess of formaldehyde in the toxoid preparation. Similar results could be obtained by using formaldehyde alone.

Further experimental work is directed to assessing the value of mixed injections of antitoxin and toxoid in incipient cases of tetanus or as a prophylactic where the threat of tetanus exists.

It is claimed from these experiments that the diminution of circulating antitoxin due to combination of toxoid and antitoxin which may follow such injections can be surmounted by using a large excess of antitoxin, and further that the presence of the antitoxin does not interfere with the function of the toxoid as an antigenic stimulus, provided injections of toxoid and antitoxin are made in separate areas of the body.

[The detailed experimental results however, show that the injections of antitoxin and toxoid in separate areas of the animal body, although they ultimately produce an adequate response, only do so to a lesser degree and after a longer period of time.]

J. W. McLeod

LEVINE, L. **The Quantitative Flocculation Reaction of Equine Tetanus Antitoxin.** *Brit. J. Exper. Path.* 1959, Aug., v. 40, No. 4, 343–57, 7 figs. [18 refs.]

ISTRATI, G. & ISTRATI, Maria. Recherches sur l'immunisation du cerveau vis-à-vis de la toxine tétanique. [**Investigations concerning the Immunization of the Brain to Tetanus Toxin**] *Arch. Roumaines Path. Exper. et Microbiol.* 1959, Mar., v. 18, No. 1, 59–75. [20 refs.]

An extensive series of experiments on the protection of mice from intracerebral injection of tetanus toxin is presented. This can be achieved by subcutaneous administration of toxoid provided a toxoid adsorbed on Al (OH_3) or alum-precipitated is used. The neutralizing capacity of normal brain tissue and of brain tissue from mice which have undergone intracerebral immunization is compared.

There is considerable neutralizing power in suspensions of normal brain tissue, 25 mgm. of suspension of brain tissue will neutralize about 90% of a small dose of toxin, *i.e.* 10 LD100; but this capacity is considerably raised in mice which have undergone intracerebral inoculation. The fact that the neutralizing power of such brain tissue is near to that of the serum of the mouse whereas in mice passively immunized with large doses of antitoxin the neutralizing power of the serum greatly exceeds that of suspensions of brain tissue is advanced as proof of local production of antitoxin in the nervous system. *J. W. McLeod*

IKIC, D. **Post-Inoculation Reactions caused by Tetanus P.T.A.P. Prophylactic with and without Addition of Typhoid and Paratyphoid Germs.** *Acta Med. Iugoslavica.* 1958, v. 12, Nos. 1/2, 103–8.

The addition of typhoid and paratyphoid bacilli to an aluminium phosphate tetanus toxoid preparation caused a greater general and local reaction but also increased response in units of tetanus antitoxin.

The number of observations on which the latter conclusion is based is rather small. *J. W. McLeod*

SAKAGUCHI, G. & SAKAGUCHI, S. **Studies on Toxin Production of *Clostridium botulinum* Type E. III. Characterization of Toxin Precursor.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 1–9, 9 figs. [13 refs.]

In a study of the toxin precursor produced by *Clostridium botulinum* type E, it was found that strains varied in the extent to which precursor was secreted and separated in the supernatant or remained attached to the bacteria. It was liberated to a much greater extent by trypsinization of the bacteria than by trypsinization of the supernatant.

In view of the fact that mechanical disintegration of the bacteria did not increase the yield, it was assumed that the situation of the precursor was related to the surface of the micro-organism.

Partial purification of the product by extraction with acetate buffer followed by ammonium sulphate precipitation and solution of the precipitate yielded material which was submitted to analysis by ultraviolet absorption and by starch electrophoresis. From these observations it is concluded that the undigested precursor is a body of acidic nature and contains ribonucleic acid. In the process of digestion, the ribonucleic acid is split off to leave a toxic product which is of neutral or basic character. In the zones of maximum concentration of toxin obtained from samples of trypsin-treated material, phosphorus was diminished and the absorption spectrum no longer gave evidence of the presence of ribonucleic acid. *J. W. McLeod*

MEISEL, H., ALBRYCHT, H. & RYMKIEWICZ, D. **Kappa Toxin in Extracts from Mechanically Disrupted Cells and Spores of *Clostridium perfringens* Type A.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 7, 259–62. [11 refs.]

Cultures of this *Clostridium, Cl. welchii*, in glucose broth yield supernatants which contain no trace of collagenase. If the bacilli are broken up by mechanical shaking with glass beads, distinct collagenase

activity is obtained which is neutralized by anti-*welchii* serum but not by anti-*histolyticum* or by normal horse serum. It was also possible to obtain the same enzyme from spores after treating these with lysozyme, desoxyribonuclease and trypsin to remove all traces of the vegetative form of the bacillus. Hence the spores also contain this ferment. *J. W. McLeod*

CHERRY, W. B. & FREEMAN, Elizabeth M. **Staining Bacterial Smears with Fluorescent Antibody. V. The Rapid Identification of *Bacillus anthracis* in Culture and in Human and Murine Tissues.** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 582–603, 18 figs. [17 (11 coloured) on 5 pls.] [26 refs.]

When antibody against *Bacillus anthracis* was conjugated with fluorescein it was found that culture smears or smears from the liver of infected mice which contained *B. anthracis* reacted with the antibody globulin in a fashion which made the demonstration of *B. anthracis* both easy and rapid. The method has possible extensions to human medicine and veterinary medicine as well as in animal experiments. Full and adequate technical details are given in this paper of the antigenic and optical methods employed. The results appear to be highly satisfactory.

J. W. Howie

LEISE, J. M., CARTER, C. H., FRIEDLANDER, H. & FREED, S. W. **Criteria for the Identification of *Bacillus anthracis*.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 655–60. [10 refs.]

The authors claim that by studying motility, haemolysis, reaction with gamma phage and the "string-of-pearls reaction" [this *Bulletin*, 1954, v. 29, 207], *i.e.* the production of enlarged round cell forms in the presence of penicillin, they are able to distinguish virulent and avirulent strains of the anthrax bacillus from *Bacillus cereus* and other aerobic sporeformers. [These findings are at variance with those of BROWN *et al.* (this *Bulletin*, 1958, v. 33, 991) whose work is criticized in some aspects.] *John R. Norris*

BARBER, Cella, ZILIŞTEANU, Eugenia & NAFTA, I. Sur les polyosides du *Bacillus anthracis*. II. Variantes "R" et "Sm". [**The Polysaccharides of *B. anthracis***] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Mar., v. 18, No. 1, 27–30.

STAMATIN, N. & LI VAN SOB. Isolement d'un bactériophage spécifique pour l'espèce *B. anthracis* et d'une souche asporogène test du *Bacillus anthracis*. [**The Isolation of a Specific Bacteriophage for the Species *B. anthracis* and of a Nonsporogenous Test-Strain of *B. anthracis***] *Arch. Roumaines Path. Expér et Microbiol.* 1959, Mar., v. 18, No. 1, 31–2.

The English summary appended to the paper is as follows:—

"1. A bacteriophage strain exerting a lytic action upon strains of the species *B. anthracis* was isolated from the soil.

"2. From the daughter-colonies of a sporogenous B. anthracis strain a nonsporogenous variant was isolated which is sensitive to the action of phages and may be used as a test-strain."

CIUCĂ, M., ZILIŞTEANU, Eugenia & NAFTA, I. La susceptibilité des souches locales de *B. anthracis* à l'égard des bactériophages "W" McCloy, "Gamma" Brown et Cherry et "E" Stamatin. [**The Sensitivity of Local Strains of *Bacillus anthracis* to W (McCloy), Gamma (Brown and Cherry) and E_1 (Stamatin) Bacteriophages**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Mar., v. 18, No. 1, 9–13.

The English summary appended to the paper is as follows:—

"The action exerted by W (McCloy), gamma (Brown and Cherry) and E_1 (Stamatin) Bacteriophages on 130 strains of *B. anthracis* was investigated. One of the strains was resistant to the action of W. gamma, and E_1 phages, four strains to the action of W and gamma phages, one strain to the action of gamma and E_1 phages, and one strain to the action of W phage only.

"Of the three phages under study, phage E_1 proved to be the most specific as regards the 130 strains investigated by us.

"None of the 25 studied strains from the aerobic spore-bearing bacilli group of the genus *Bacillus* displayed a clear-cut sensitivity to one of the three phages used."

PATOCKA, F.; SCHINDLER, J.; MÁRA, M. **Studies on the Pathogenicity of *Listeria monocytogenes*. I. Protein Substance isolated from Cells of *Listeria monocytogenes* enhancing Listeric Infection** [PATOCKA, SCHINDLER & MÁRA]. *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 7/8, 573–85, 9 figs. [20 refs.] **II. Influence of Substances isolated from Cells of *Listeria monocytogenes* on Experimental Listeriosis in White Mice.** [PATOCKA, MÁRA & SCHINDLER]. *Ibid.*, 586–93, 5 figs. [14 refs.]

A strain of *Listeria monocytogenes* isolated from a case of human listeriosis was grown in 1% glucose meat broth in 5-litre flasks at 37°C. for 18–24 hours. A 10% suspension (wet weight) of washed centrifuged organisms was made in a 1 M glycine solution, incubated at 37°C. for 24 hours, shaken with sterile sand for 12 hours, centrifuged, and finally dialysed against tap water at 13°C. The lysate was now precipitated successively with methanol and ammonium sulphate and dialysed with tap water. After 0·94% NaCl was added to the non-dialysable fraction, it was centrifuged and the solution contained the active principle. The extract, when injected intraperitoneally into white mice along with an infective dose of *L. monocytogenes*, lowered the LD50 as compared to controls. The extract was effective only when injected simultaneously with the organism. The extract had no effect on experimental brucellosis or on streptococcal and staphylococcal infections. Although the extract was not

lethal on injection to rabbits, guineapigs, or white mice, its intradermal injection into rabbits gave rise at the injection site to an inoculation erythema, a nodule with firm infiltration lasting 3–4 days. Histologically this was shown to be an inflammatory reaction. Intravenous injection gave a febrile response with leukocytosis reaching a peak 4 hours after injection in rabbits, and 3 days in mice injected intraperitoneally. The extract did not produce in rabbits haemorrhagic necrosis after epinephrine nor a local Shwartzman reaction nor did it give a generalized Shwartzman reaction in a rabbit receiving 30 mgm. of cortisone for 3 successive days. Heating at 55°C. for 20 min., and at 60°C. for 60 min. lowered the activity of the extract, boiling completely destroyed activity, precipitation with 15% TCA [trichloracetic acid ?] also completely inactivated the extract. The active principle appears to be a protein or a complex associated with a protein. Polysaccharides, nucleic acids, and lipids are also present. The amounts of these were reduced and the protein content increased by repeated precipitation of the glycine lysate with either methanol or ammonium sulphate. The activity of this more purified extract was equal to or only slightly higher than that of the glycine lysate. Although the authors were unable to obtain a pure homogeneous preparation from the organisms, they consider that the activity is not linked to either cell nucleo-proteins or to a cellular endotoxin of the Boivin type.

In the second paper various components of the bacterial cells were prepared and examined for their virulence-enhancing activity in *Listeria* infections. With HIRST and LANCEFIELD's method for the extraction of streptococcal M-protein, a protein named L-protein was extracted from the previously described glycine lysate. There were still traces of polysaccharides and nucleic acids present. After purification these L-protein preparations showed in mouse experiments activity within the significance of the previous findings. There was variation in the activity of individual batches of L-proteins, but on average this activity was lower than that of the glycine lysate extract. L-proteins gave slight antibody production but not of the H or O type. Nucleo-protein preparations were inactive; an attempt to isolate an endotoxin analogous to that of Boivin was unsuccessful; a polysaccharide isolated from the cells also had no significant effect on enhancing the virulence of *L. monocytogenes*.

Elizabeth M. Harper

BRILL, J., MIKULASZEK, E. & TRUSZCZYNSKI, M. Immunochemische Untersuchungen über die Antigen-Struktur des *Erysipelotrix rhusiopathiae*. [**Immunochemical Investigations on the Antigenic Structure of** *Erysipelotrix rhusiopathiae*] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 558–69, 1 fig. [10 refs.]

The English summary appended to the paper is as follows:—

"The chemical and serological investigations described indicate, that two polysaccharid haptens are among the antigens of Erysipelotrix rhusiopathiae. The chemical structure and the serological specificity of both haptens are different. One of these haptens (C_1) is coupled to protein and forms a protein-polysaccharid complex, moreover, it is also found in the nucleo-protein fraction. The other polysaccharid (C_2) seems to be liberated from the bacterial cell wall by the action of alkaline compounds. Using the technique described, both haptens are precipitated as lipopoly-saccharids. Chiefly the polysaccharid C_1 is responsible for the type specificity of Erysipelotrix rhusiopathiae."

WIGAND, R. Morphologische, biologische und serologische Eigenschaften der Bartonellen. [**Morphological Biological and Serological Characteristics of** *Bartonella*] With an introduction by E. G. NAUCK. pp. xi + 95, 14 figs. [247 refs.] 1958. Stuttgart: Georg Thieme Verlag. [13s. 7d.]

FUNGI

MARIAT, F. Sur la culture de la phase levure de la souche singe *d'Histoplasma capsulatum*. [**Attempts at Cultivation of the Yeast Phase of the Monkey Strain of** *Histoplasma capsulatum*] *Ann. Inst. Pasteur*. 1959, Aug., v. 97, No. 2, 254–8, 5 figs. on pl.

After repeated attempts to obtain yeast-phase cultures of *Histoplasma* from a number of strains isolated from spontaneously infected African monkeys and from experimentally inoculated animals the author twice succeeded in obtaining slow-growing cultures at 37°C. on Kurung medium in which distinct yeast-like forms were observable. On the first occasion they developed in the third sub-culture (the intervals between sub-cultures ranging from 2 to 5 months). The yeast cells thus obtained measured on the average 8μ in diameter. They were relatively few in number and were interspersed in an irregular and vesiculated type of mycelium. The author was, however, unable to maintain this yeast-phase in culture. On the second occasion he obtained the yeast-phase in primary culture from a mesenteric gland of an experimentally infected hamster. This he was able to maintain until the third sub-culture when it was replaced by a very irregular and very much vesiculated type of mycelium. The author concludes from these results that the transformation of mycelial to yeast phase in the case of the monkey strain of *Histoplasma* can be brought about only with the greatest difficulty when conditions which enable this transformation to occur quite easily in the case of classical *Histoplasma capsulatum* and the variety *duboisii* are provided. *C. J. La Touche*

GADEBUSCH, H. H. **Phagocytosis of** *Cryptococcus neoformans* **in Anemic Mice.** *J. Bacteriology*. 1959, Aug., v. 78, No 2, 259–62, 1 fig.

"Enhancement *in vitro* and *in vivo* of phagocytosis by 'anemic' mouse polymorphonuclear leucocytes was shown with reference to the small capsule variant of *Cryptococcus neoformans* strain RE. No such increase

in activity could be demonstrated with *C. neoformans* strain 3723 or the large capsule variant of strain RE.

"Anemic mice injected with the large capsule variant of the RE strain demonstrated a statistically significant prolongation in the onset of the disease when compared with control animals and this effect has been ascribed to increased macrophage activity."

NOVÁK, E. K. **The Utilization of Malonate by** *Candida albicans*. *Acta Microbiologica*. Budapest. 1959, v. 6, No. 2, 117–23, 4 figs. [33 refs.]

PINE, L. & HARDIN, H. *Actinomyces israelii*, **a Cause of Lacrimal Canaliculitis in Man.** *J. Bacteriology*. 1959, Aug., v. 78, No. 2, 164–70, 3 figs. [24 refs.]

"Two strains of the genus *Actinomyces* have been isolated from cases of lacrimal canaliculitis and conjunctivitis of the eye. Although their colonies are smooth, these strains have cultural and morphological characteristics which would characterize them as *Actinomyces israelii*. However, one strain ferments glucose forming large amounts of propionic acid. Propionic acid was not formed by several other strains of Actinomyces studied previously."

PEPYS, J. **Allergic Hypersensitivity to Fungi.** *Postgraduate Med. J.* 1959, Aug., v. 35, No. 406, 436–40, 469. [32 refs.]

BACTERIOPHAGES

DE VICENTE JORDANA, R. **Study on Adsorption of Bacteriophage by Filters.** *Applied Microbiol.* Baltimore. 1959, July, v. 7, No. 4, 239–47, 7 figs. [28 refs.]

It is well known that whether a virus passes through a filter or is retained depends not only upon the size of the virus and the size of the filter pores, but also upon such physico-chemical factors as temperature and pressure, and the ionic strength and *p*H of the virus suspension. The author has tested the effect of these variables on the filtration of a coliphage and a phage from *Bacillus polymyxa* through Chamberland candles, sintered glass plates and Seitz EK asbestos pads. A negligible amount of phage adsorbed on to sintered glass and Chamberland filters over a range of *p*H 5·0–7·8, but a loss occurred with Seitz filters, the loss becoming smaller with more alkaline *p*H. Chamberland filters when dirty adsorbed phage, but not after being cleaned by heating to white heat. Pre-saturation of Seitz pads with phage reduced adsorption, and there were better yields when bigger volumes were filtered through smaller pads. For example; with a 6 cm. asbestos pad and a suction pressure of 650 mm. mercury, all the phage was adsorbed when 10 ml. was filtered at *p*H 5·9, while minimum adsorption occurred when 50 ml. was filtered at *p*H 6·85.

About 2% of filtrates from Seitz filters were contaminated from unknown causes. Contamination arose most often when there was too much foaming, when the screw nuts holding the pads were loose, and when more than a week had elapsed between sterilization of the filters and their use.

The author concludes that viruses can be isolated by means of filters, provided adequate precautions are taken. *Janice Taverne*

TOUSSAINT, A. J. & MUSCHEL, L. H. **Neutralization of Bacteriophage by Normal Serum.** [Correspondence.] *Nature*. 1959, June 27, v. 183, 1825–7. [10 refs.]

The ability of normal serum to neutralize bacteriophage has been attributed to its properdin content, although (a) there is not always a correlation between neutralizing titre and properdin level [BARLOW *et al.*, this *Bulletin*, 1958, v. 33, 992] and (b) with some sera, the neutralizing activity against one kind of phage is not correlated with its activity against others [COWAN, *ibid.*, 1959, v. 34, 180]. Cowan suggested therefore, that properdin might be a family of cross-reacting antibodies which can also combine with zymosan. Work is described here which shows that the neutralizing activity of normal human serum against different T phages is markedly specific (the properdin system is essentially non-specific in its action), and is independent of properdin content.

About 25 T2 or T5 phage particles per cell were adsorbed to *Escherichia coli* B and the preparations formolized and used to absorb serum. The neutralizing activity of serum against the phage used to absorb it was found to be almost completely removed, without any change in the ability to neutralize heterologous phage. Absorption with bacteria free of phage did not alter phage neutralization titres. Thus specific antibody appears to be responsible for phage neutralization.

Phage neutralization by normal serum appears to be independent of properdin for the following reasons: (1) absorption of serum with *E. coli* reduced the properdin level without causing any change in the phage neutralizing titre. (2) absorption with cells having adsorbed phage did not reduce the properdin level (or that of haemolytic complement) any further, and (3) the amount of properdin left in phage-absorbed serum was within normal limits, yet no neutralizing activity against homologous phage remained.

It is of interest that normal serum from "germ-free" guineapigs neutralized T2, and to a greater extent than serum from ordinary animals of the same strain. The levels of haemolytic complement and properdin were normal although gamma globulin was barely detectable by paper electrophoresis. Viruses cannot be excluded from animals reared in a "germ-free" environment, and it is possible that these, or an antigen in the animals' food, stimulated the production of antibody which cross-reacted with the phage. *Janice Taverne*

CORTESE, M. Sull'inattivazione da properdina dei fagi della serie T. **[Studies on Phage Neutralization by Properdin]** *Giorn. di Microbiol.* Naples. 1958, July–Dec., v. 6, Nos. 1, 2 & 3, 1–9, 1 fig. [12 refs.]

The English summary appended to the paper is as follows:—

"The properdin system, comprised of properdin, all

components of complement and magnesium, was demonstrated by Van Vunakis *et al.*, to be responsible for the capacity of fresh human serum to inactivate T_2 phage, and T_2 phage neutralization was proposed as an indicator of properdin levels in sera.

"Virucidal activity of normal serum containing properdin has been tested against the seven phages of the T series. T_7 resulted more sensitive than T_2, T_5, T_1, T_3, T_4, and T_6 phages. The phage T_7 neutralization may be used to assay for properdin as well as T_2.

"It was also demonstrated that by quick cooling the virucidal activity of fresh serum persists practically unaltered, while the gradual freezing does not make stable the phage-neutralizing factors of serum."

LOVELESS, A.; STOCK, Jocelyn C. **The Influence of Radiomimetic Substances on Deoxyribonucleic Acid Synthesis and Function studied in *Escherichia coli*/Phage Systems. II. Properties of Coliphage *T2* treated with Di(2-chloroethyl)-methylamine** [LOVELESS & STOCK]. *Proc. Roy. Soc.* Ser. B. 1959, Sept. 1, v. 150, No. 941, 486–96, 1 fig. [11 refs.] **III. Mutation of *T2* Bacteriophage as a consequence of Alkylation *in vitro*: the Uniqueness of Ethylation** [LOVELESS]. *Ibid.*, 497–508, 8 figs. [15 refs.]

II. T2 phage inactivated by treatment with di (2-chloroethyl) methylamine (HN 2) was studied. Treated phage adsorbed to *Escherichia coli* B cells at the same rate as untreated phage, but its host-killing ability was reduced. There was no difference in antibody blocking power between phage inactivated by HN 2 and by UV-irradiation. Multiplicity reactivation occurred to a small extent, and marker rescue experiments with superinfection with a host range mutant gave similar results. DNA released by subjecting treated phage to osmotic shock had a lower viscosity than that from untreated phage.

Thus T2 inactivated by HN 2 has the same properties as T2 exposed to X-rays. It has been proposed that X-rayed phage cannot multiply because it fails to inject its DNA into the host bacterium and the authors consider that this is also the probable explanation of the inactivation of T2 by the "radiomimetic" agent HN 2. [See also this *Bulletin*, 1958, v. 33, 1185.]

III. A series of alkylating agents were tested to see if they increased the number of plaque-type and host range mutants produced by T2 phage. Phage was treated with approximately equivalent doses of the different agents and adsorbed to *E. coli* B cells before plating. Only 2 alkylating agents, ethyl methane sulphonate and di-ethyl sulphate, appeared to be mutagenic, and both act by introducing ethyl groups into the phage. Treated phage had the same latent period and average burst size as untreated phage. It is considered that the increased mutation rate is a direct consequence of the chemical treatment, although the ethylation itself does not constitute the mutation. It is not known why ethylation was effective but not other alkylations.

[For part I, see this *Bulletin*, 1959, v. 34, 1186.]

Janice Taverne

MAHLER, H. R. & FRASER, D. **Studies in Partially Resolved Bacteriophage-Host Systems. IV. Some Properties of the Protoplast-Infecting Agent derived from T2 Bacteriophage.** *Virology.* New York. 1959, Aug., v. 8, No. 4, 401–24, 7 figs. [32 refs.]

KOCH, A. L. **The Dynamics of Coliphage Plaque Formation. I. Macroplaque Experiments.** *Virology.* New York. 1959, July, v. 8, No. 3, 273–92, 4 figs. [18 refs.]

VIRUSES

In this section the abstracts are arranged as far as possible in the following order:—General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

BRODA, E. and FRISCH-NIGGEMEYER, W. [Edited by]. **Proceedings of the Fourth International Congress of Biochemistry.** Vienna, 1–6, September, 1958. Vol. 7, Symposium 7. pp. xi+255, illustrated. 1959. New York. Paris. Los Angeles. London: Pergamon Press Ltd., 4 & 5 Fitzroy Square, W. 1. [63s.]

This symposium mainly covers studies of the nucleic acids of plant, animal and bacterial viruses and of related problems. It is of interest mainly to the expert in these fields, although there are a few useful reviews of long term studies, notably J. W. BEARD *et al.* (pp. 99–118) on avian leukaemia viruses, C. E. SCHWERDT (pp. 130–41) on the purification and physical properties of poliovirus, and M. A. LAUFFER (pp. 167–84) on the inactivation of viruses (based on tobacco mosaic virus) by heat, formalin and X-rays.

The first 12 papers are devoted to tobacco mosaic virus (TMV); there is a short paper by G. H. BERGOLD (pp. 95–98) on the structure and chemistry of some insect viruses; 10 papers on animal viruses follow—5 of them on myxoviruses; the symposium ends with 5 papers on bacteriophage. *C. E. Gordon Smith*

KOPROWSKI, H. **Importance of Genetics of Viruses in Medical Research.** *Amer. J. Human Genetics.* 1959, June, v. 11, No. 2, Pt. 2, 335–51, 3 charts. [52 refs.]

This is a readable account of what is known about the genetics of viruses of medical importance, rather than a discussion of the value of this knowledge to medicine. Historically, the most obvious hereditary character of a virus, and the one on which workers concentrated, was its pathogenicity for man. The aim was to modify virulence while retaining immunizing power. JENNER had paved the way with vaccinia, and later PASTEUR with rabies. The next achievement was the production, by laboratory manipulation, of a stable variant of yellow fever virus, the 17 D strain. It is pointed out that early work of this kind was characterized by its unpredictability. Because of the techniques

available, the virus populations selected were necessarily heterogeneous.

The first purposeful attempt at analysis of the heritable characters of an animal virus was made by BURNET, who studied the change in influenza virus from the human form to the laboratory form which occurs upon cultivation in the chick embryo. A search for genetic markers followed, characters which it was hoped could be used in investigating the genetic constancy of a given virus strain, and the problem of virus mutation. Examples are given of some of the markers known for pox viruses, such as pock size, mouse virulence, haemagglutinin production, and some for poliomyelitis virus, such as plaque size, heat resistance and relation to presence of cystine in the culture. Advances with this last virus were made possible by the plaque technique of DULBECCO and VOGT [this *Bulletin*, 1956, v. 31, 701] by means of which the progeny of a single virus particle can be isolated. Earlier, mutation and attenuation had been studied by adapting a virus to a new host and, after repeated passage, looking for avirulent strains. Recently the method has been to pick plaques and then study the neuropathogenicity of the clones selected. For instance, it has been found that for some strains of poliomyelitis virus a low efficiency of plating under acid agar is associated with a low virulence for the monkey nervous system. However, the rate of back mutation *in vitro* is not comparable with that *in vivo*, where reversion to virulence has been found after one passage through the human gut. It seems that there is little value in comparing delicate quantitative genetical analysis with the results of blind inoculation into the spinal cord where the mode of infection and multiplication is unknown. The author stresses the fact that animal virologists notoriously disregard the genetics of the host.

In a section on recombination in animal viruses the author records the confusion there has been in the case of influenza. The results of mixed infection obtained by some workers may have been genuine recombination, but others have obtained heterozygotic hybrids, which did not retain their identity on subsequent passage. Hybrids derived from double infection with poliomyelitis virus he considers may have resulted from phenotypic mixing, a phenomenon not easy to distinguish from heterozygosis. True genetic recombination has, however, been obtained between strains of herpes simplex virus, and with the pox viruses.

The paper ends with an account of experiments done on viruses stripped of their protein coats. Infectious RNA has been extracted from a number of mammalian viruses, although the infectivity did not exceed 0·1% of that of the original virus suspension. The different properties of intact virus and of isolated virus RNA are summarized. It is in this field, the author believes, that most promise for the future lies. The role of the protein coat of the virus should be elucidated. Recombination experiments between 2 different RNA preparations will become possible. Chemically defined markers may become available instead of genetic markers. But in spite of these exciting possibilities, it remains painfully clear how little we known about the reason a virus grows in one host and not another, and about adaptation, virulence and attenuation. *Janice Taverne*

DMOCHOWSKI, L. **Viruses and Tumors. An Old Problem in the Light of Recent Advances.** *Bact. Reviews.* 1959, Mar. v. 23, No. 1, 18–40. [198 refs.]

The present paper is a review article in which the author gives a survey of the literature concerning the relationship between tumours and viruses from 1908 until the present time. Although no known infectious virus can give rise to a malignant condition it is not possible to draw any distinction between infectious and tumour-producing viruses on the basis of morphological, biochemical or immunological studies. The period from 1908 to 1918 was marked by the discovery of the virus origin of chicken leucosis and sarcoma. During the next decade the virus aetiology of human warts was established, and between 1928 and 1948 further malignant neoplasms of virus origin were discovered, but the main development of the subject has only taken place during the last 10 years, with the discovery of the mouse mammary tumour and leukaemia viruses, and much of the success achieved has been due to the use of newborn mice as experimental animals. By means of the electron microscope it has been possible to observe particles of mouse mammary tumour virus, and particles resembling viruses have been found in mice with induced and spontaneous leukaemia. Virus particles can also be observed in avian neoplasms, and the method is now being extended to the investigation of human leukaemia and other malignant conditions. *D. J. Bauer*

MILES, J. A. R. **Latency in Viruses.** *Australian J. Sci.* 1958, Dec., v. 21, No. 5a, P137–P145. [38 refs.]

CROSS, R. C., HARDING, H. B. & HEPLER, Opal E. **Certain Quantitative Aspects in the Fixation of Complement by Viral Antigens and Antibodies.** *Amer. J. Clin. Path.* 1959, Feb., v. 31, No. 2, 117–27, 5 figs. [32 refs.]

In an investigation of the quantitative aspects of the fixation of complement by virus antigens studies have been made of the haemolysis curves obtained with fixed amounts of complement and immune serum and varying amounts of antigen, and also with a fixed amount of antigen and varying amounts of immune serum. In experiments of this type carried out with eastern equine encephalomyelitis, mumps, influenza B, psittacosis and rickettsialpox antigens a sigmoid curve was obtained when the percentage of haemolysis was plotted against the amount of antigen or of antiserum, which was transformed into a straight line between the limits of 20% and 80% haemolysis when the percentage of haemolysis was converted to logarithms. The possibility of using these results for the quantitative determination of virus antigens is discussed. *D. J. Bauer*

BARSKI, G., CORNEFERT, Francine & WALLACE, Roslyn E. **Response of Ciliated Epithelia of Different Histological Origin to Virus Infections *in vitro*.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 407–11, 2 figs. [10 refs.]

In a continuation of previous work [this *Bulletin*, 1958, v. 33, 410] an investigation has been made of the

resistance of ciliated epithelium growing in plasma clot cultures to the cytopathic effect of certain viruses. In cultures of human Fallopian tube the ciliated cells in the fragments retained their activity for 20–25 days, and occasional ciliated cells were observed in the epithelial outgrowths. After infection with poliomyelitis, Mengo, infectious bovine rhinotracheitis and type 1 adenovirus the ciliated cells remained unaffected for several days after the dedifferentiated cells had been destroyed. A similar delay was observed in cultures of rabbit Fallopian tube and trachea infected with herpes virus. The delay in appearance of the cytopathic effect was not reduced by abolishing the action of the cilia with nembutal, or by treating the cells with tryspin or hyaluronidase.

D. J. Bauer

Döhner, L. Über die Herstellung eines Hydrolysates aus Molkeneiweiss für Gewebekulturen. [**Production of a Hydrolysate of Milk Protein for Tissue Cultures**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, July–Aug., v. 5, No. 4, 225–30, 2 figs [13 refs.]

Bedson, S. P. The Harben Lectures, 1958. **The Psittacosis-Lymphogranuloma Group of Infective Agents. Lecture I. The History and the Characters of these Agents.** *J. Roy. Inst. Pub. Health & Hyg.* 1959, Mar., v. 22, No. 3, 67–78. [34 refs.] **Lecture II. The Position of the Agents of Trachoma, Inclusion Conjunctivitis and Cat-Scratch Disease. The Ecology of the Agents of the Psittacosis-Lymphogranuloma Group.** *Ibid.*, Apr., No. 4, 99–112. [41 refs.] **Lecture III. The Diagnosis, Treatment and Control of Infection of Man with these Agents. The Taxonomic Position of the Group.** *Ibid.*, May, No. 5, 131–43, 1 pl. [34 refs.]

These 3 lectures provide a comprehensive and well-balanced review of the development of our knowledge of the psittacosis-lymphogranuloma agents by one of those who independently shared in the original demonstration of the viral origin of psittacosis in 1930 and who has taken a leading part in later studies of these agents. The historical introduction describes the pandemic of " parrot fever " in 1929–30 and the early work which culminated in the isolation of psittacosis virus. The main features of this agent are described as a preamble to general discussion of the characters of other members of the group of " closely related species similar in size, staining and microscopic appearance, possessing in common a heat-stable antigen, but distinguished from each other to some extent by their natural host range and pathogenicity for experimental animals, and in final issue by the possession of a specific antigen ". The author supports his thesis that psittacosis virus multiplies by binary fission with cogent arguments based on the morphological appearances of stained preparations of infected tissue and of thin-sections studied by electron microscopy, the development of swollen forms of virus under the suppressive action of penicillin (which resemble the effects of this antibiotic on sensitive bacteria as a result of inhibition of cell-division), and the growth-curve of psittacosis virus which failed to show an " eclipse phase " in the author's experiments.

The second lecture opens with a common-sense discussion of classification of these agents. The recent cultivation of trachoma virus has enabled further evidence to be added to serological and morphological observations which justify inclusion of this agent, and that of inclusion conjunctivitis, in the psittacosis-lymphogranuloma group. The scanty data yet available about cat-scratch disease scarcely warrant its definite inclusion in the same group.

After discussing the ecology of the widely-distributed avian and mammalian viruses of the psittacosis-lymphogranuloma group, the author speculates on the possible evolution of non-avian strains from ancestral psittacosis-ornithosis virus which exists in more balanced partnership with its avian hosts than do the mammalian viruses with theirs. The features of human infections are summarized with emphasis on the variability of severity and duration of illness due to avian viruses of the group. The sources of infection of man are discussed: disease may be an occupational risk of exposure to non-psittacine and domestic birds including poultry and pigeons. Viruses from psittacine birds may cause more severe disease. Man-to-man transmission of avian viruses is unusual and there is little evidence of the existence of psittacosis strains adapted to man.

Laboratory diagnostic methods are considered in the third lecture. Further work is required to elucidate the anomalous incomplete cross reactivity between psittacosis and lymphogranuloma venereum in skin sensitivity tests with group antigen (Frei test). For treatment of disease, Aureomycin and oxytetracycline are the most effective chemotherapeutic agents available. Banning the importation of psittacine birds into countries where they are not indigenous is a logical and useful control measure, as shown by the outbreaks of human disease shortly after the temporary lifting of the embargo in Britain, New Zealand, and New York State in 1952.

In a final discussion of taxonomy, the author argues that the psittacosis-lymphogranuloma agents occupy an intermediate position between the larger true viruses of the pox group and the metabolically more independent rickettsiae with which they share sensitivity to certain antibiotics.

[It is impossible to summarize adequately these very readable lectures which are packed with information and enlivened by the author's views on controversial aspects of his subject.] *N. R. Grist*

Pearce, J. M. & Weeks, D. **The Suppression of Lesions and the Development of Immunity by means of Antihyaluronidase in Vaccinia and Fibroma Infections.** *Amer. J. Path.* 1959, Mar.–Apr., v. 35, No. 2, 233–47, 5 figs on 2 pls.

A suspension of Shope fibroma virus was mixed with a preparation of a hyaluronidase inhibitor obtained from bovine or human umbilical cords and injected intradermally in rabbits, and the size of the tumours which developed was recorded and compared with those of control inoculations of virus and saline. The mean volume of 40 tumours developing from virus mixed with inhibitor was 0·2 cc., whereas the mean volume of 40 tumours of the control series was 2·9 cc. Treatment of the virus with hyaluronidase inhibitor did not depress

the subsequent formation of neutralizing antibody. In similar experiments with vaccinia virus the inhibitor retarded the development and reduced the severity of the lesions, without affecting the development of neutralizing antibody. *D. J. Bauer*

PELMONT, J. & MORGAN, H. R. Facteurs nutritifs influençant la croissance du virus de l'herpès dans la souche de cellules L de Earle. [**Nutritional Factors influencing the Growth of Herpes Virus in the Strain L Cells of Earle**] *Ann. Inst. Pasteur.* 1959, Apr., v. 96, No. 4, 448–54.

The MF strain of herpes virus could be adapted to growth in L cells cultured in a medium containing yeast extract, lactalbumin hydrolysate and horse serum; in the initial passages growth was poor, but by the 16th passage the virus had become adapted and multiplied to high titres. L cells placed in a synthetic medium consisting of amino-acids, water-soluble vitamins and salts survived for a long time without showing signs of multiplication; when cells maintained under these conditions were infected the virus multiplied as well as in cultures supplied with growth medium. When cells were maintained in Earle solution and then infected no multiplication of virus occurred but a latent infection had evidently taken place, since growth of virus would occur if the cells were then transferred to growth medium. By varying the composition of the synthetic medium it was found that phenylalamine, tryptophan, arginine, threonine, leucine, valine and histidine were required for virus multiplication, whereas isoleucine, lysine, alanine, glycine and glutamine could be omitted from the medium.
D. J. Bauer

FINKELSTEIN, R. A., ALLEN, R. & SULKIN, S. E. **Inhibition of Herpes Simplex Virus by Normal Serum: its Relationship to the Properdin System.** *J. Infect. Dis.* 1959, Mar.–Apr., v. 104, No. 2, 184–92, 5 figs. [33 refs.]

In experiments with 8 strains of herpes simplex virus it was found that the infectivity of the virus in TCD50 for HeLa cell cultures could be reduced by 2–3 log units by incubation with normal rat serum for 1 hour at 37°C. No inactivation was produced by normal rat serum heated at 56°C. for 30 minutes, but removal of the properdin content by treatment with zymosan reduced the inhibitory effect by 2 log units, and a similar effect was produced when the serum was treated with an ion-exchange resin in order to remove magnesium ions. The resistance of the virus to inhibition could not be increased by serial passage in the presence of normal rat serum. The virus could be inhibited by a purified preparation of human properdin, provided that complement in the form of properdin-deficient guineapig serum was added. Inhibition of the virus by normal rat serum did not take place at temperatures below 30°C., and multiplication of the virus in HeLa cell cultures was not affected when normal rat serum was added 1–3 hours after infection.

As a result of these observations the authors suggest that recurrent outbreaks of herpes simplex infection in the same patient may be due to periodic depressions in the serum properdin level. *D. J. Bauer*

STOKER, M. G. P. & NEWTON, Alison. **The Effect of Herpes Virus on HeLa Cells dividing Parasynchronously.** *Virology.* New York. 1959, Apr., v. 7, No. 4, 438–48, 5 figs. [11 refs.]

HeLa cells placed at 4°C. for 1 hour and then incubated at 37°C. will divide almost synchronously after 18 and again after 36 hours (WILDY and NEWTON, *Biochem. J.*, 1958, v. 68, 14P), and in the present work the effect of infection with herpes virus upon this phenomenon has been studied. When such cultures were infected with virus in a multiplicity of 1·1 plaque-forming unit per cell 4 hours before the expected time of division no increase in cell number could be observed, whereas cells similarly treated with virus neutralized by antiserum divided at the expected time. Inhibition of mitosis was still observed when virus was added 1½ hours before the expected time of mitosis, but virus which became adsorbed without initiating infection failed to inhibit mitosis. The rate of virus growth in cultures dividing parasynchronously did not differ from that occurring in untreated cultures in which the cells were dividing asynchronously. *D. J. Bauer*

FARNHAM, Ann E. & NEWTON, Alison A. **The Effect of Some Environmental Factors on Herpes Virus grown in HeLa Cells.** *Virology.* New York. 1959, Apr., v. 7, No. 4, 449–61, 7 figs. [20 refs.]

In an investigation of the rate of adsorption of herpes virus onto HeLa cell monolayers it was found that adsorption took place at equal rates at 4°, 30° and 37°C. The amount of virus adsorbed was reduced by 5 log units when adsorption was carried out in 0·25M sucrose solution instead of phosphate-buffered saline. The penetration of the virus after adsorption was studied by removing the medium at various times after infection and replacing it with medium containing immune serum; after 2 hours at 37°C. the cells were washed 3 times with phosphate-buffered saline and incubated for 3 days in maintenance medium, after which the plaques which had developed were counted. The results showed that when infection was carried out at 37°C. all the virus which became adsorbed had become insusceptible to neutralization by antibody after 3–4 hours, but penetration was greatly reduced in extent at 30° and at 4°C. The growth rate of the virus and the yield were also studied at various temperatures. At 32°C. the virus grew more slowly than at 37°C., but the total yield was greater on account of the lesser degree of thermal inactivation at the lower temperature. In experiments in which the *p*H of the culture fluid was varied between 6 and 7·5 the maximum yield of virus was obtained at *p*H 7·0–7·5. *D. J. Bauer*

CANTELL, K. **Investigations on Mumps Virus. Propagation of Mumps Virus in Chick Embryos during Serial Allantoic Passages with Undiluted Inocula.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1959, v. 37, Suppl. 1, 84 pp., 21 figs. [178 refs.]

An investigation has been made of the serial passage of mumps virus in the allantoic cavity with undiluted infected allantoic fluids as the inoculum, and also

allantoic fluid diluted to 10^{-4}–10^{-6}. During 22 passages of the Enders strain with diluted inocula high haemagglutinin titres were always obtained after 5 days of incubation, whereas during the same number of passages with undiluted inocula haemagglutinin could not be detected in one-third of the passages. Similar results were obtained with the Habel strain and 2 other strains of mumps virus, and also when the incubation period for each passage was reduced to 2 and 3 days. The infectivity titre remained high during the first 3 passages with undiluted inocula and then declined by about 5 log units as far as the 10th passage; a parallel fall was observed in the infectivity-haemagglutinin ratio, which later became indeterminate when haemagglutinin could no longer be detected. High haemagglutinin titres could be obtained in passage by diluting fluids which had given low titres when inoculated in the undiluted state, and the suppression of haemagglutinin production was therefore due to autointerference. The production of haemagglutinin after the inoculation of diluted fluid could also be suppressed by subsequently inoculating the eggs with an undiluted fluid.

In a final discussion attention is drawn to the similarity between these results and those obtained by VON MAGNUS with influenza virus [this *Bulletin*, 1953, v. 28, 292]. *D. J. Bauer*

RUSSELL, P. K. & MORGAN, H. R. **Mumps Viral Cytolysin. I. Action on Human Epithelial Cells in Tissue Culture.** *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 38–40, 2 figs.

Cultures of a number of different cell lines were grown for 4–8 days, washed in Parker medium No. 635 to remove traces of human serum and incubated in the same medium for a further period of 24 hours. After removal of the medium, mumps virus in the form of infected allantoic fluid diluted 1:4 in the same medium was added to the cultures, which were then incubated and observed at intervals over a period of 24 hours. In cultures of human conjunctival, kidney, liver and intestinal cells the onset of cytolysis was observed after 3 hours; the granularity of the cytoplasm disappeared, the nuclei increased in size and the cell membranes became indistinct and disappeared, giving an appearance suggestive of giant cells. The effect was not observed in cultures treated with virus which had been inactivated by heating at 60°C. for 30 minutes. L cells were resistant to cytolysis. *D. J. Bauer*

RODRIGUES-DA-SILVA, G. & FELDMAN, H. A. **Formalin treated Chicken Erythrocytes as Indicators of Influenza A Virus (Asian) and its Antibody.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 241–5. [14 refs.]

Methods are described for the preparation of chicken erythrocyte suspensions and their use in haemagglutination and haemagglutination-inhibition tests with Asian influenza virus. Tests performed with formalin-treated cells stored over a period of 3 months gave reproducible results comparable to those obtained with fresh cells. *H. G. Pereira*

PRIMAVESI, K. A. Der Nachweis des Hepatitisvirus durch charakteristische Veränderungen in der Leber von Hühnerembryonen. [**The Detection of Hepatitis Virus by means of Characteristic Changes in the Liver of Chick Embryos**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 5, 461–70. [22 refs.]

Fertile eggs at the 9th–11th day of incubation were infected on the dropped chorioallantoic membrane with blood, bile or stools from patients suffering from infective hepatitis, and after further incubation for 3–4 days the embryos were subjected to histological examination. The livers were frequently enlarged and friable, and green or dark brown in colour, but changes of similar extent were also seen in control embryos. On microscopical examination there was diffuse and focal round cell infiltration, degeneration of the liver epithelium and proliferation of histiocytes. These changes were seen in experiments with 9 of 29 samples of material in which nearly 150 embryo livers were examined, and were not found in 80 control embryos inoculated with saline; in control examinations of material from healthy persons they were observed in 2 of 14 samples of bile but not with 13 sera and 11 stool filtrates. *D. J. Bauer*

ŽÁCKOVÁ, Zdenka, JASTROWOVÁ, Ilse & ŽÁCEK, K. Komplement-fixační antigen u lymfocyární choriomeningitidy, připravený bentonitovou purifikací. [**Lymphocytic Choriomeningitis Complement-Fixing Antigen prepared by Bentonite Purification**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 3, 153–6. English summary (5 lines).

Guineapigs were infected intracerebrally and subcutaneously with lymphocytic choriomeningitis virus, and when symptoms of encephalitis had developed the animals were exsanguinated and the spleens were removed and made into a 40% suspension with saline. The suspension was left overnight at 4°C., clarified by low-speed centrifugation and mixed with an equal volume of a 1% suspension of bentonite prepared 24–48 hours previously. The mixture was left at 4°C. for 1 hour and then centrifuged at low and high speed. The final supernatant fluid was then used as complement-fixing antigen. In tests with guineapig hyperimmune sera the bentonite antigen gave the same antibody and antigen titres as a preparation of soluble antigen made by Smadel's method. The antigen was not anticomplementary, and in control tests with 162 Wassermann-positive sera 8·5% of unspecific positive results were obtained, compared with 6·7% in similar tests with soluble antigen. *D. J. Bauer*

BLOOM, H. H., MACK, W. N., KRUEGER, B. J. & MALLMANN, W. L. **Identification of Enteroviruses in Sewage.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 61–8. [16 refs.]

The results of examining over 1,000 samples of sewage collected from Lansing and East Lansing, Michigan, from September 1955 to October 1857 by inoculation of monkey kidney tissue cultures or suckling mice are

reported. A virus was isolated from about 15% of the samples, and the method is considered to be one of great value in assessing the prevalence of enteroviruses in the community. A comparison was made of the results obtained in this study with those obtained by other workers [GELFAND *et al.*, this *Bulletin*, 1958, v. 33, 1024; HONIG *et al.*, this *Bulletin*, 1956, v. 31, 613] who have carried out large-scale surveys of the flora of normal children. The results are closely similar so that sewage sampling appears to be a reliable and more satisfactory method of determining the viral flora.

Many more isolations were made from East Lansing than from Lansing and this difference is ascribed to the large quantity of industrial waste present in Lansing sewage. Samples were taken during the course of treatment through the sewage works and whereas the raw sewage yielded 14 viruses from 43 samples the final effluent only yielded 4 viruses from the 41 samples. The incidence of ECHO viruses was highest in October whereas the incidence of Coxsackie A viruses was highest in August. Poliovirus type 1 and type 3 and 9 of the first 14 types of ECHO virus were among the viruses isolated. The exact details of the technique of collection of sewage samples are given and it is noted that the results are superior to those described by KELLY *et al.* [this *Bulletin*, 1957, v. 32, 1006]. This superiority is ascribed to the fact that the viruses were recovered from this sewage by ultracentrifugation rather than by ion exchange resin adsorption and elution. *A. J. Beale*

GELFAND, H. M. **The Incidence of certain Endemic Enteric Virus Infections in Southern Louisiana.** *Southern Med. J.* 1959, July, v. 52, No. 7, 819–27, 4 figs. [12 refs.]

GELFAND, FOX and their co-workers [this *Bulletin*, 1958, v. 33, 931, & 1024; *ibid.*, 1959, v. 34, 112] have added greatly to the precision of our knowledge of the spread of poliovirus under natural conditions by carrying out detailed and well conceived longitudinal studies of infection in a group of families in Southern Louisiana. The faecal samples and sera collected from 115 index (newborn) children in the period 1953–56, and sera from their families, were examined for enteroviruses. 4 patterns of incidence of antibodies with age were noted. Coxsackie B2 and 4, ECHO 7 and 9, like poliovirus, show a rapid acquisition of antibodies early in life, and about 80% of adults had antibodies. Coxsackie B5 and ECHO types 1 and 2 show a very flat curve of incidence which is about 10% at 1 year rising to about 30% at 35 years. Coxsackie A9 and B1 and 3 form an upper intermediate group, and ECHO 6, 8 and 12 a lower intermediate group. In the group of viruses showing a high incidence of antibodies in a family every child older than the youngest with antibodies has them whereas in the lower groups skips of antibodies occur in older children and for the lowest incidence group these skips are the rule rather than the exception.

Isolations of viruses indicate that members of each of the previously mentioned groups are closely similar —all having a high incidence. The explanation for the differing antibody patterns is sought by postulating that the antibodies to the lower group (Coxsackie B5 ECHO 1 and 2) are lost very rapidly. During the 3 years 613 viruses were isolated from the 115 children by using monkey kidney cells. The highest number of isolations from 1 child was 11 and only 1 child escaped detectable infection. There was an epidemic of ECHO 7 infection involving over one-third of the children. Neither in this epidemic nor with the other viral isolations was there any evidence of disease being caused by these agents, but their prevalence—over one-third of the children at any time were excreting viruses —illustrates the caution necessary in ascribing aetiological significance to virus isolations from patients with disease. 128 of the isolates remain to be identified. All the agents except ECHO 10 (which is anyway odd man out in the enterovirus family, being associated with respiratory disease) were more prevalent in the summer and early autumn months. [SABIN (*Science*, 1959, v. 130, 1387) has suggested that the ECHO 10 group of viruses be reclassified as Reoviruses.] *A. J. Beale*

DARNELL, J. E., Jr. & SAWYER, T. K. **Variation in Plaque-Forming Ability among Parental and Clonal Strains of HeLa Cells.** *Virology.* New York. 1959, June, v. 8, No. 2, 223–9, 2 figs.

2 HeLa cell lines and pure clones derived from them were compared for plaque-forming ability when infected with type 1 poliovirus. It was found that a previously uncloned stock HeLa cell culture (HeLa I) and pure clones derived therefrom consistently gave more (up to about 8 times) plaques than the S3 strain (of PUCK and FISHER, *J. Exper. Med.*, 1956, v. 104, 427). Virus was adsorbed more quickly to the more sensitive cells, but the difference was inadequate to explain the discrepancies in titre of virus. The plaque size differed in different cell strains, but plaque size was not correlated with degree of sensitivity to virus. The relatively resistant cells were "epithelial" whereas the resistant ones were "fibroblastic" in appearance. It is noted that VOGT and DULBECCO (*Virology*, 1958, v. 5, 425) have described relatively resistant cultures which were fibroblastic in appearance. *A. J. Beale*

DEKEGEL, D. **Comparative Study of Aerobic Glycolysis by Different Cell Strains in Tissue Culture. Possible Relation between Poliomyelitis Virus Susceptibility and Glycolytic Metabolism.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 27–32, 2 figs. [15 refs.]

A variety of continuous cell lines have been derived from both normal and malignant tissues. Since many of these continuous cell lines closely resemble one another in morphology and in antigenic structure the question has arisen as to whether those continuous cell lines derived from normal tissues have acquired malignant properties in culture. WARBURG *et al.* (*Ztschr. f. Naturforsch.*, 1958, v. 13B, 61) have suggested that a distinctive property of malignant cells is a high rate of aerobic glycolysis. A study was made, therefore, of the aerobic glycolysis of a variety of tissue culture

cells and it was found that the majority (for example, HeLa and KB cells derived from malignant tumours and the cell lines derived by CHANG from normal tissues (*Proc. Soc. Exper. Biol. & Med.*, 1954, v. 87, 440)) whether derived from normal or malignant tissue, shared the property of a high rate of aerobic glycolysis. On the other hand some continuous cell lines, for example, a uterine fibroblast U 12, described by SWIMM and PARKER (*Anatomical Record*, 1956, v. 124, 499) and the altered monkey kidney cells described by PARKER *et al.* (*New York Acad. Sci., Special Publication*, 1957, v. 5, 303) did not show any aerobic glycolysis. These cells also shared the property of not being sensitive to poliovirus infection. *A. J. Beale*

WENNER, H. A., ARCHETTI, I. & DUBES, G. R., with the technical assistance of P. KAMITSUKA, Margaret LENAHAN, Jean WESTON, Eleanor SHARP & Margaret CHAPIN. **Antigenic Variations among Type 1 Polioviruses. A Study of 16 Wild-Type Strains and 5 Variants.** *Amer. J. Hyg.* 1959, July, v. 70, No. 1, 66–90, 4 figs. [32 refs.]

16 wild strains (all purified by isolation from single plaques) of type 1 poliovirus and 5 variants obtained from 1 of the strains (Akron) were examined for antigenic differences. Antisera obtained by inoculating 1 dose of antigen into both rabbits and monkeys were employed with the inhibition of the cytopathic effect of poliovirus as the end point (CP test). Monkey sera were also employed for metabolic inhibition (MI test) titrations of neutralizing antibody and for complement-fixation tests. A few sera were also tested by determining the dilution of serum giving a 90% reduction in virus plaque count. The results are presented in full and are analysed. They showed that all the strains (from widely separated parts of the globe) are closely related sharing major antigens. They can, however, be distinguished by minor but significant antigenic differences. All the variant strains derived from Akron appeared to be closely similar by the most accurate plaque method.

There appeared to be no relation between virulence for monkeys of the strains and the antibody titres produced in the animals. The fact that the relatively avirulent cold-adapted strains of Akron are antigenically closely similar to the virulent wild type indicates that such attenuated strains might be useful for vaccination. The preponderant shared antigenic components of type 1 virus explain the success of poliovaccine, but some of the strains show quite marked differences from the strains which are incorporated in vaccine (type 1 Brunhilde or Mahoney). It is thus possible that type 1 strains sufficiently different from the vaccine strains may explain some vaccine failures.

No evidence of antigens shared between the poliovirus types was obtained. None of the monkey antisera to the type 1 strains neutralized the MEF 1 type 2 strain or the Saukett type 3 strain.

[These results are similar to those previously reported by the authors for type 2 virus (WENNER *et al.*, this *Bulletin*, 1957, v. 32, 513). They also confirm results for type 1 virus obtained by MCBRIDE (*ibid.*, 1959, v. 34, 833) using the more refined method devised by DULBECCO *et al.* (*ibid.*, 1956, v. 31, 959). The antigenic differences within the 3 types of poliovirus should prove a valuable marker both in epidemiological and genetic studies of poliovirus.] *A. J. Beale*

DUBES, G. R., ARCHETTI, I. & WENNER, H. A., with the technical assistance of P. KAMITSUKA, Jean WESTON, Margaret LENAHAN, Eleanor SHARP & Margaret CHAPIN. **Antigenic Variations among Type 3 Polioviruses.** *Amer. J. Hyg.* 1959, July, v. 70, No. 1, 91–105, 1 fig. [11 refs.]

This paper records an antigenic analysis for type 3 poliovirus strains similar to that undertaken by the same workers for the type 1 and 2 strains [this *Bulletin*, 1957, v. 32, 513; see also above]. Quite marked antigenic differences were found between the 9 type 3 polioviruses studied. 5 strains of Leon and 2 of Mantova virus were found to have only minor antigenic differences which may not be significant. All the virus strains were purified by 3 serial single plaque isolations. The third isolate was rapidly passed to prepare antigen for the preparation of antisera in monkeys and the performance of the neutralization (CP for all strains and MI and plaque reduction for a few strains) and complement-fixation tests. The limitation of this procedure was revealed in attempts to obtain pure stocks of turbid plaque variants of Leon and Mantova strains. Virus grown from such turbid plaques even after repeated picking of single plaques always produced a proportion of clear plaque mutants. The monkey kidney cell culture system offered a selective advantage to the clear plaque variants. These variants were also found to be much less virulent for monkeys by the intramuscular route than the turbid plaque producers. *A. J. Beale*

IONESCU-MIHĂIESTI, C., HORODNICEANU, F., SERGIESCU, Dina & KLEIN, R. Studiu comparativ al serurilor antipoliomielitice de referintă preparate pe animale mici de laborator. [**A Comparative Study on Reference Poliomyelitis Antisera prepared in Small Laboratory Animals**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1959, Jan.–Feb., v. 4, No. 1, 25–30. English summary (9 lines).

Antisera to the 3 types of poliomyelitis virus were prepared in rabbits, guineapigs and mice, which were given 6 intramuscular injections of infected HeLa cell culture fluid over a period of 3 weeks, followed 3 weeks later by an intraperitoneal booster injection; volumes of 5, 2 and 0·2 ml. were used for the 3 animal species respectively. The titres of the sera were then determined in neutralization tests. With the pooled sera of 5 rabbits a titre of 5,120 was obtained with type I virus, 1,280 with type II and 320 with type III, and with the pooled sera of 30 guineapigs the titres were 160, 1,280 and 640 respectively. In both species the type III antisera showed some cross-neutralization with type II virus. With the pooled sera of 50 mice titres of 320, 160 and 320 were obtained, and no cross-neutralization between types II and III was observed. *D. J. Bauer*

HALONEN, P., ROSEN, L. & HUEBNER, R. J. **Homologous and Heterologous Complement Fixing Antibody in Persons infected with ECHO, Coxsackie and Poliomyelitis Viruses.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 236–41. [15 refs.]

The cross reactions between the members of the Enterovirus group first 20 types (ECHO types 1–20, Coxsackie B1, 3, 4 and 5 and polioviruses types 1–3) were studied in complement-fixation tests with all these viruses as antigen and a series of paired human sera obtained from persons infected with ECHO 10, 16 and 20, Coxsackie B3 and polio type 1 viruses. Cross reactions were observed between the various viruses tested, particularly between ECHO types 2, 4, 5, 6, 7, 8, 11, 14, 16, 20, Coxsackie B types 1, 3, 4 and 5. ECHO 10 virus seemed unique; there were no cross reactions with the sera from adults who had been experimentally infected with ECHO 10 virus, or between ECHO 10 antigen and the other sera. This reinforces other evidence that ECHO 10 virus is not a member of the Enterovirus family [HSIUNG, this *Bulletin*, 1959, v. 34, 506]. The results confirm the fact that the complement-fixation test is not particularly valuable as a specific diagnostic tool in Enterovirus infections. Other authors have observed the cross reactions between other members of this group of viruses [for example, JOHNSSON *et al.*, *ibid.*, 1959, v. 34, 27].

A. J. Beale

MAYER, V. Lipotropismus von Coxsackie-Virus (Typ B-1) bei ausgewachsenen weissen Mäusen. [**Lipotropism of Coxsackie Virus (Type B1) in Weaned White Mice**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 282–7, 1 fig. [18 refs.]

Mice weighing 9–11 gm. were infected subcutaneously with the Conn-5 and Klíč strains of B1 Coxsackie virus, and the virus content of the brown fat and other tissues at intervals after infection was determined by titration in infant mice. The titre of virus in the brown fat attained a maximum of 4·5–5·7 log units 2 days after infection and then declined; the titre in the pancreas attained 6·5 log units after 4 days, and a lesser rise of titre was observed in the blood, liver, brain and myocardium.

D. J. Bauer

BELL, J. F. & HADLOW, W. J. **Responses of Newborn and Adult Domestic Rabbits (*Oryctolagus*) to Infections with Coxsackie Viruses.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 54–60, 4 figs.

A study was made of the effect of Coxsackie groups A and B on suckling rabbits. An attempt was made to prepare antisera in adult rabbits against those Coxsackie types that grew to high titre in suckling rabbit muscle. None of the Coxsackie A or B strains caused any illness in the suckling rabbits but many of the strains grew to high titre in them (A1, 2, 3, 4, 5, 6, 8, 9, 10). The highest titres were obtained with Coxsackie A3, 4, 5 and 8 and these viruses caused the most extensive skeletal muscle degeneration. Skeletal muscle degeneration was the only histological lesion that was seen in the suckling rabbits; even the group B viruses failed to show lesions in other tissues, for example, the nervous system, brown fat or pancreas. With strains of Coxsackie A virus that grew to high titre in the suckling rabbits good antisera were obtained in adult rabbits against many of the types. This method is somewhat unreliable but when successful appears to give very satisfactory antisera.

A. J. Beale

CAJAL, N., MATEESCU, S. & COPELOVICI, Y. **Susceptibility of Adult Mice to the Pathogenic Action of Coxsackie Virus following Ionizing Irradiation (X and β).** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 107–12. [12 refs.]

Adult mice are not susceptible to Coxsackie group A virus infection. However, X-irradiation (a single dose of 600r) or β-irradiation (50 microcuries of ^{32}P intraperitoneally) rendered suckling mice susceptible to Coxsackie A2 infection intracerebrally. 4 to 12 days after inoculation 82% of the X-irradiated and 66% of the mice treated with ^{32}P suffered from lethargy going on to paralysis and death. Coxsackie A2 was isolated from brain suspensions. Virus reached higher titre and persisted for longer in the tissues of X-irradiated or β-irradiated mice than in control adult mice after infection with Coxsackie A2 virus.

A. J. Beale

HENDERSON, J. R. & TAYLOR, R. M. **Arthropod-Borne Virus, Plaques in Agar Overlaid Tube Cultures.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 257–9. 1 fig.

Tube cultures of trypsinized Pekin duck kidney, rhesus monkey kidney and chick embryo tissue were infected, washed and overlaid with agar. Virus infections which do not cause cytopathic effects in tubes without overlay, may cause plaque formation in overlaid tubes. Arborviruses of groups A, B and C have been used, but cannot be distinguished by plaque size or shape. Group A give plaques in 2–3 days in chick-embryo tissue; Group B in 5–6 days in Pekin duck kidney; and Group C in 6–7 days in monkey kidney. The plaque determinations gave in most instances higher titres than suckling mouse titrations. The method was successfully used to perform neutralization tests.

C. E. Gordon Smith

HARDY, F. M. **The Growth of Venezuelan Equine Encephalomyelitis Virus in Various Tissue Cultures.** *Amer. J. Hyg.* 1959, July, v. 70, No. 1, 21–7, 4 text figs. & 6 figs. on pl. [21 refs.]

12th egg-passage virus was used in 8 types of tissue culture: Chang's human liver and conjunctiva, monkey kidney, chick-embryo fibroblasts, embryo mouse lung, guineapig kidney, L cells and Maben cells. All supported growth of Venezuelan equine virus, but the conjunctiva cells only when infected with large doses. The virus growth curve was similar in all, reaching a maximum 24–72 hours after infection. The majority

of cultures showed cytopathic effects in 48 hours. 1 of 5 L cell monolayers were infected by 1 mouse intracerebral LD50 of virus, but cytopathic effects occurred only when much larger doses were used.

C. E. Gordon Smith

GOMES, Gilda & CAUSEY, O. R. **Bussuquara, a New Arthropod-Borne Virus.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 275–9.

Blood from a sentinel howler monkey (*Alouatta beelzebul*) in Belém, Brazil, was inoculated intracerebrally into 3-day-old mice, some of which sickened on the 6th day. From these an agent was isolated which, between the 2nd and 5th mouse passages, showed a titre around 10^{-8} intracerebrally or intraperitoneally in suckling mice with a minimum survival time of about 4 days, and 10^{-7} intracerebrally in adult mice with a minimum survival time of about 6 days.

3 days after the original blood specimens, virus was again isolated from the blood of the monkey which sickened 16 days later and died with marked jaundice. The monkey liver had lesions compatible with yellow fever.

A saline-extract of mouse brain was used as a complement-fixing antigen in a test against pools of antisera to various arboviruses; it reacted only with the group B pool. A haemagglutinin was prepared from suckling mouse brain and tested against a variety of arbovirus antisera. Reactions were obtained with all the group B arboviruses included in the test.

Cross complement-fixation tests with rather low-titre antigens demonstrated cross-reactions of low degree with St. Louis encephalitis, Ilheus, bat salivary gland and SA H 336 viruses. With the sera of animals bled 7–10 days after infection, cross haemagglutinin-inhibition tests showed low-level cross reactions with 5 group B arboviruses. In a limited study, cross neutralization tests showed a significant cross reaction only between Bussuquara and bat salivary gland virus.

Bussuquara appears to be a new virus in Casal's group B of arboviruses only distantly related to other members of the group. *C. E. Gordon Smith*

LIBÍKOVÁ, H. **Viruses of the Tick-Borne Encephalitis Group in HeLa Cells.** *Acta Virologica.* Prague. 1959, v. 3, Suppl., 41–50, 13 figs. on 3 pls. [22 refs.]

8 strains of Russian spring-summer (RSS) group viruses were grown in HeLa cells: (1) Sofin strain of RSS encephalitis virus, (2) Belyanchikov strain of biphasic meningoencephalitis virus, (3) OGL strain of Omsk haemorrhagic fever virus, (4) 2 strains from Czechoslovakia, and one each from Hungary, Poland and Slovenia of RSS encephalitis virus. All grew in HeLa cells without difficulty causing cytopathogenic effects which could be neutralized by specific antiserum. The cytopathogenic effect did not affect all the cells, but only a high proportion of them. The pathogenicity of the strains for mice was unaffected by 20 passages in HeLa cells. *C. E. Gordon Smith*

GRESÍKOVÁ-KOHÚTOVÁ, M., with the technical assistance of A. STYKOVÁ. **Effect of pH on Infectivity of the Tick-Borne Encephalitis Virus.** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 159–67, 3 figs. [11 refs.]

Experiments were undertaken to find out whether Russian spring-summer encephalitis virus excreted in milk would survive in acid dairy products. 2 strains of virus were tested for survival over a *p*H range from 1·65 to 11·87 at intervals of 24 hours and 1 to 3 weeks. The mixtures were held at 4°C. Optimum survival with little or no loss of titre was found at *p*H between 7·0 and 9·0 (7·6–8·2 for the Hypr strain). For a period of 24 hours the viruses were very insensitive to *p*H—titres of over 10^{-3} were found after 24 hours at *p*H 2·75 and 11·55. An experiment was also made with virus stored in sour milk and it appeared to persist at a level infective intracerebrally for mice for 24–48 hours.

[For previous studies see this *Bulletin*, 1959, v. 34, 202, 401.] *C. E. Gordon Smith*

LIBÍKOVÁ, H. & VILCEK, J. **A Simple Neutralization Test for Viruses of the Tick-Borne Encephalitis Group, depending on a Complete Cytopathic Effect in HeLa Cells. (Preliminary Report.)** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 181–4, 2 figs. on 2 pls.

Where HeLa cells are infected with viruses of the Russian spring-summer group after growth of the cells in tubes, the cytopathic effect usually involves only a proportion of the cells, making the reading of tests difficult. By infecting the tubes immediately after putting the cells into the tubes, growth is inhibited by the presence of virus. Growth of a cell layer and the concomitant change in the *p*H of the nutrient fluid indicates absence of infective virus. This can be used in a neutralization test. *C. E. Gordon Smith*

ŽÁCKOVÁ, Zdenka & ŽÁCEK, K., with the technical assistance of I. JASTROWOVÉ. Některé problémy jednodušší a bezpečnější přípravy encefalitických komplementfixačních antigenů. [**Some Problems of the Simpler and Safer Preparation of Encephalitis Complement-Fixing Antigens**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 2, 84–90, 2 figs. & 1 graph. English summary.

A study has been made of Czech tick-borne encephalitis virus complement-fixing antigens prepared by various methods from infected mouse brains. 36 batches of antigen prepared by 3 or 5 extractions with acetone and ether had a satisfactory titre, and 9 batches prepared by a single extraction with ether had lower titres but were still satisfactory for use. 22 batches prepared by a single extraction with bentonite gave high titres of unspecific fixation and were unsuitable for use. The closed system used for ensuring safety during the manipulations involved in preparing the antigen is illustrated in 2 figures. *D. J. Bauer*

SMITH, C. E. G. & WESTGARTH, D. R. **The Use of Survival Time in the Analysis of Neutralization Tests for Serum Antibody Surveys.** *J. Hygiene.* 1957, June, v. 55, No. 2, 224–38, 2 figs. [13 refs.]

Surveys of human and animal sera for the presence of antibodies to anthropod-borne neurotropic viruses are commonly carried out by the serum neutralization test in mice. Initially the LD50 titre of seed virus is determined by conventional assay methods after which a dose, usually of 100 × LD50, of the virus is mixed with the undiluted sera under test and incubated. Each group of 6 mice is then inoculated with one of the serum-virus mixtures and after an appropriate period of observation the number of deaths in each group is observed. It is customary to disregard all animals which die within 4 days of inoculation and to count as deaths all mice which are paralysed at the end of the observation period. Mortality ratios (deaths/inoculated) of 0/6, 1/6, 0/5 and 1/5 are termed "positive", ratios of 6/6, 5/6, 4/6, 5/5 and 4/5 are termed "negative" and all other possible ratios are considered "equivocal".

The major difficulties encountered in this test arise because the ratios, each based on at most 6 mice, result in a discontinuous scale of response and because the required dose of virus is not easily achieved. It is of some interest to note that in 163 tests in which SMITHBURN *et al.* required doses of 100 × LD50 they only achieved doses within the range of 50 × LD50 and 200 × LD50 in 47% of the tests [this *Bulletin*, 1954, v. 29, 890, 891, 1267]. Both these difficulties result in a lack of precision and necessitate many repeat tests; consequently a new method, based on a survival time response, is proposed.

It has been shown by other workers [*ibid.*, 1940, v. 15, 741; 1951, v. 26, 950] that an approximate rectilinear relationship exists between the log dose of a virus administered to a group of mice and the mean of the reciprocals of their survival times in days. The survival time index proposed for a group of K mice is

$$Y = \frac{1000}{K} \sum_{i=1}^{K} \frac{1}{ti}$$

where t_i is the number of days survived by the ith mouse in the group. As in the earlier procedure, mice dying within 4 days of inoculation are ignored and mice paralysed on the last day of observation are counted as deaths on that day. However, for reasons which are given, survivors at the end of the period of observation are counted as deaths on the 42nd day. The procedure and calculations are described in detail and cannot be adequately summarized.

The interpretation of the results is based upon a "t" test of significance comparing the mean survival time index for the control, Y_o, with that of the unknown serum, Y_t. Thus for a predetermined significance level 4 possible types of result may be considered. First, Y_t may be significantly less than Y_o; such results are regarded as "positive" and are not repeated. Second, Y_t may be equal to, or less, though not significantly, than Y_o; such results are normally repeated and regarded as "equivocal". Third, Y_t may be greater, though not significantly, than Y_o and fourth, Y_t may be significantly greater than Y_o; both the third and the fourth types are regarded as "negative" and for reasons of economy not repeated, although it is realized that the third may include some positive results.

Difficulties that can arise in the proposed test are discussed and ways of reducing the equivocal range are suggested. In a series of repeated tests on 229 sera there were 144 positives at the first determination and only 5 of these were negative when the determination was repeated. In the same series, only 1 of the 18 negatives at the first determination was found to be positive at the second. In another series of some 615 observations the incidence of such sign reversal was only 2·6%.

It is suggested that the advantages of the proposed method are that (1) it is based on a predetermined level of significance, (2) it gives consistent and comparable results over a wide range of virus doses, (3) it is as economical as other methods in time and animals and (4) the calculations are simple and yield more information per animal than do the methods of quantal response. *E. A. Cheeseman*

WAGNER, R. R., SNYDER, Ruth M., HOOK, E. W. & LUTTRELL, C. N. **Effect of Bacterial Endotoxin of Resistance of Mice to Viral Encephalitides, Including Comparative Studies of the Interference Phenomenon.** *J. Immunology.* 1959, July, v. 83, No. 1, 87–98, 8 figs [30 refs.]

Lipopolysaccharides extracted from certain microorganisms have been shown to protect animals against bacterial infections, but to have no direct antibacterial action.

Purified lipopolysaccharide (AE) prepared from *Salmonella abortus equi* was used. Very little protection was detected when 1–5 μgm. of AE was given to mice 24 hours before intracerebral challenge with eastern equine encephalomyelitis virus. Intracerebral AE gave very little protection against intraperitoneal challenge with eastern equine virus, but intravenous AE protected 40% of the mice inoculated (30) compared with 10% survivals in controls. When 5 μgm. of AE was given intraperitoneally in addition to 1 μgm. intracerebrally, only 7 of 20 mice were protected compared with 2 of 20 controls, but the median survival time of treated mice was 3 days longer than that of the controls. Estimations of the virus growth curves in these experiments showed only slight differences between AE-treated and controls, except with intraperitoneal, and more so with intraperitoneal + intracerebral AE, when there were differences in the number of mice in which virus multiplication could be detected. Protection was also demonstrated when the AE was given simultaneously with the challenge virus, when it was given in 5 spaced doses after challenge and, when given in 2 doses before and 2 after challenge.

AE did not influence the growth of eastern equine virus in tissue culture.

Slight degrees of protection were also demonstrated with AE against challenge with encephalomyocarditis virus.

Marked protection by interference was demonstrated when WS influenza virus was given intracerebrally 24 hours before challenge with eastern equine virus. Intraperitoneal WS virus gave much less protection. Interference between WS influenza and eastern equine virus was marked in tissue culture, (contrasting with the effect of AE). Interference between WS and encephalomyocarditis virus occurred when both were administered intracerebrally, but not if they were given intraperitoneally. *C. E. Gordon Smith*

KHEMANI, K. M. & JHALA, H. I. **Study of Rabies Virus Tropism for Salivary Glands.** *Indian J. Med. Sci.* 1959, May, v. 13, No. 5, 420–22.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1230.]

PLACIDI, L. Note sur l'incubation prolongée ou la latence du virus rabique. Cas de la souche Flury. Observation et discussion. [**Prolonged Incubation Period, or Latency of Rabies Virus. Study of the Flury Strain. Observation and Discussion**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 265–7.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1230.]

MÖBEST, H. Über die Schutzwirkung des Hempt-Impstoffes gegen Tollwut bei verkürzter Immunisierung und vorverlegter Nachinjektion. [**The Protective Effect of Hempt Vaccine against Rabies with Abbreviated Immunization and Early Booster Injection**] *Arch. f. Hyg. u. Bakt.* 1959, Feb., v. 143, No. 2, 135–9.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1231.]

NICOLAU, S. S., DRAGANESCO, N., NICOLAU, C. S., FUHRER, B., GIRD, E. & IONESCO N. I. **A New Type of Anti-Rabies Vaccine; Investigations into the Migration of the Vaccine Virus in the Animal Organism by means of Radioactive Substances.** *Acta Virologica.* Prague. 1959, v. 3, Suppl. 91–6, 1 fig. [16 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1231.]

YURKOVSKY, A. M. & GHENDON, Y. Z. **A Study on the Content of Neutralizing Antibodies in Protein Fractions of Hyperimmune Horse and Bovine Rabies Antisera.** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 153–8. [14 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1232.]

HOSTY, T. S., KISSLING, R. E., SCHAEFFER, M., WALLACE, G.A. & DIBBLE, E. H. **Human Antirabies Gamma Globulin.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1111–19.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1232.]

COLLIER, W. A., DE ROEVER-BONNET, H. & HOEKSTRA, J. **A Neurotropic Variety of the Vaccine Strain 17D.** *Trop. & Geograph Med.* Amsterdam. 1959, Mar., v. 11, No. 1, 80–92, 4 graphs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1229.]

COLLIER, W. A., DE ROEVER-BONNET, H. & HOEKSTRA, J. **Changed Virulence of the Yellow Fever Virus Vaccine Strain 17D by a Single Mouse Passage.** *Trop. & Geograph. Med.* Amsterdam. 1959, Mar., v. 11, No. 1, 75–9, 5 graphs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1228.]

MATUMOTO, M., NISHI, I. & SABURI, Y. Multiplication de la souche neurotrope du virus de la fièvre de la Vallée du Rift dans la rate et dans le foie de la souris. [**Multiplication of Neurotropic Rift Valley Fever Virus in Mouse Liver and Spleen**] *C. R. Soc. Biol.* 1958, v. 152, No. 11, 1623–6, 2 figs.

Mice were infected intraperitoneally with neurotropic Rift Valley fever virus and titrations of the virus content of various organs were made at intervals after infection. Virus could be found in the blood, lungs and kidneys for 3–4 days after infection, in the liver for 5–8 days, and in the spleen for up to 21 days. Neutralizing antibody appeared in the blood after 3–5 days. The virus still retained its neurotropic character after 14 intraperitoneal passages from spleen material. *D. J. Bauer*

JUNGEBLUT, C. W. & KODZA, Helen. **Interference between Certain Neurotropic Viruses in Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 270–75, 2 figs. [15 refs.]

Col SK virus does not produce cytopathic effects on L cells but prior treatment of the cells with high concentrations of this virus interfered with the subsequent challenge of the cultures with EMC virus. Similarly Col SK virus does not cause cytopathic effects on HeLa cells although the virus is adsorbed to these cells and undergoes at least one cycle of multiplication in them. Large doses of Col SK virus (about 10^7 mouse infectious doses) in a particular strain of HeLa cells were found to interfere with the growth of several strains of poliovirus and with Coxsackie B5. Interference was less marked in another strain of HeLa cells and in a continuous line of human amnion cells. Interference did not appear until after 4 hours' incubation of the cells with Col SK virus, and was prevented if adsorption of Col SK virus to the cell surface was inhibited by the pre-treatment of the cells with RDE. Heating Col SK virus destroys the interfering capacity and infectivity at the same rate. If HeLa cells are infected with Col SK virus and then washed after a 4-hour adsorption period the supernatant fluid fails to act as an interfering agent until the appearance of new virus in high titre occurs at about 12–24 hours. The authors

note that the site of action of the Col SK interference is at present unknown; it may be at the cell surface or intracellular. It is unlikely, perhaps, that it occurs at the cell surface since the cell receptors for Col SK but not for poliovirus are destroyed by the enzyme RDE. *A. J. Beale*

LIEBENOW, W. & SCHMIDT, D. **Isolation of Infectious Ribonucleic Acid from the Brains of Mice infected with M-M Virus.** *Acta Virologica.* Prague. 1959, July, v. 3, No. 3, 168–71, 1 fig.

"An infectious nucleic acid was obtained by phenol extraction of mouse brains infected with MM-virus. In order to show that infectivity was not caused by residual intact virus, both virus and nucleic acid solutions were subjected to different tests. Total inactivation of the RNA preparation followed ribonuclease treatment, whereas it caused no loss of infectivity in the virus preparation. Treatment of the RNA with deoxyribonuc'ease or trypsin had no effect. Incubating the RNA preparation at 37°C. for 3 hours destroyed its infectivity completely, whereas the same treatment did not cause any significant change in the virus. No protein could be demonstrated in the RNA preparation by the biuret reaction. The absorption curve of RNA had a characteristic maximum at 260 mμ. The average value of the N : P ratio was determined as 1.84.

"MM-virus was found to be extraordinarily resistant to alcohol. Precipitation of virus by three volumes of alcohol caused a decrease in infectivity at most of 2 logarithms, but the same treatment caused no losses of infectivity of RNA. Proof that animals injected with RNA actually came down with a MM-infection was given by neutralization of material derived from these animals by MM-antiserum."

POPE, J. H. **A Virus of the Encephalomyocarditis Group from a Water-Rat, *Hydromys chrysogaster*, in North Queensland.** *Australian J. Exper. Biol. & Med. Sci.* 1959, Apr., v. 37, Pt. 2, 117–24. [28 refs.]

"A virus, referred to as the Innisfail strain, was isolated by mouse inoculation from a naturally infected water-rat, *Hydromys chrysogaster*, captured in north Queensland, Australia. It was shown to be indistiguishable from the EMC virus of Helwig and Schmidt by cross-neutralization and cross-complement fixation tests, and was considered to belong to the EMC group of viruses.

"Mice and guinea-pigs were highly susceptible. Rats showed signs of paralysis, but usually survived. Rabbits and three-day-old chickens were resistant.

"Infection of mice was characterised by paralysis and death in 2–3 days, and encephalitis and myositis were the prominent histopathological features. Heavily infected guinea-pigs died within 3–7 days, with encephalitis and severe macroscopic myocarditis.

"This is believed to be the first report of natural infection with a virus of the EMC group in Australia.

"*Toxoplasma* was also isolated from the water-rat, making a new host record."

IMMUNITY

DUBOS, R. J. & SCHAEDLER, R. W. **Nutrition and Infection.** *J. Pediatrics.* St. Louis. 1959, July, v. 55, No. 1, 1–14. [56 refs.]

Reviews of this subject are more numerous than papers reporting good original work. Nevertheless, this one may be welcomed because it keeps well clear of vague generalities and helpfully ignores a great many papers which ought never to have been published. The terms "nutrition" and "infection" lack scientific precision, although they have been used in many untenable generalizations. So far as generalizations may be tenable in this subject, it might appear worth emphasizing that a well fed animal is not necessarily, on account of its diet, as well equipped to overcome certain infections as a poorly fed animal. The best diet for growth and reproduction is not necessarily the best for promoting resistance to infection. Dietary influences on resistance to infection, moreover, even when they are clearly demonstrable under defined experimental conditions, may be obscured by stronger hereditary influences affecting either host or parasite. But real dietary effects can be shown and they may become clearly demonstrable after much shorter periods of feeding than had hitherto been supposed.

[This review, which clearly displays the superior merit of selection over comprehensiveness, deals mostly with important papers published in the last 15 years. It gives clear accounts of and precise references to work which shows clear dietary effects on particular infections.] *J. W. Howie*

LEDERBERG, J. **Genes and Antibodies. Do Antigens bear Instructions for Antibody Specificity or do they select Cell Lines that arise by Mutation?** *Science.* 1959, June 19, v. 129, 1649–53. [40 refs.]

In recent years most theories of antibody formation have assumed that the antigen conveys instructions to the organism which result in the production of specific antibody globulin (instructive theories). Other theories can be based on the assumption that the organism already possesses the information needed for the synthesis of any given antibody and that the antigen acts as a selective stimulus to the production of specific globulin (elective theories). In this paper an elective theory of antibody formation is expounded in the form of 9 propositions, each of which is discussed in detail.

The key proposition (No. 5) is that antibody-producing cells, with no previous experience of antigen, spontaneously produce small amounts of antibody corresponding to their own genotype.

The first 4 propositions suggest a way in which a sufficient variety of genotypes to account for the range of antibodies which an organism can produce might arise. It is postulated that at some stage in the proliferation of the precursors of antibody-producing cells a high rate of mutation occurs in the form of random assembly of nucleotides in the DNA of the "globulin gene". If each pattern of nucleotides determines a unique sequence of amino acids in antibody globulin on

which its specificity depends, then a variety of antibody-producing cells should result, each with the capacity to produce a single antibody.

The last 4 propositions attempt to account for the familiar features of the immune response taking as starting point the existence of a great diversity of cells, each spontaneously producing small quantities of a specific antibody. Immune tolerance is explained in terms of suppression of maturation of the immature cell by the antigen-antibody combination. The primary response is attributed to stimulation of protein synthesis and cell maturation in the more mature cell by the antigen-antibody combination. The secondary response is assumed to be the result of genetically stable mature cells proliferating extensively under antigenic stimulation, thus generating large clones of cells able to produce homologous antibody. Permanent immunity would result from the persistence of such clones after the disappearance of the antigen. *R. B. Morrison*

SHEWELL, Jennifer & LONG, D. A. **The Influence of the Thyroid Gland on Antitoxin Production in Different Species.** *J. Hygiene.* 1959, June, v. 57, No. 2, 202–9. [17 refs.]

Groups of guineapigs, rats, mice, rabbits were given subcutaneous injections of L-thyroxine (BDH) twice a week for 3–6 weeks—the doses being 0·1 mgm./kgm. body weight for guineapigs, 0·02 mgm./kgm. for rats, 0·2 mgm./kgm. for mice, and 0·5 mgm./kgm. for rabbits. These induced thyroid hyperactivity. Comparable groups of animals had their thyroid activity reduced (a) by the addition of *n*-propylthiouracil in 3% cane sugar in the drinking water—intake 200 mgm./kgm. body weight per day; (b) by surgical thyroidectomy; and (c) by radiothyroidectomy—2 doses of 1 mc. of ^{131}I sodium iodide in saline being injected intraperitoneally at 1 week's interval.

All the experimentally treated animals were subsequently immunized with either tetanus or diphtheria alum precipitated toxoid. 2 injections, with a 28-day interval, of 2·5 Lf/kgm. body weight of toxoid were given.

Thyroxine raised the antitoxin levels in guineapigs but lowered the levels in rats, mice, and rabbits, the difference in titres between normal control and experimentally treated guineapigs, rats and rabbits being statistically significant; in mice the difference was of borderline significance.

Propylthiouracil raised the antitoxin levels in rats and mice compared with the controls, whereas guineapigs had lower levels than controls. Again these results were statistically significant. With rabbits there was no change in the levels between control and experimental animals.

Surgical thyroidectomy and radiothyroidectomy in guineapigs resulted in a slight decrease of antitoxin levels—of borderline significance, whereas rats and mice showed markedly higher levels than controls.

The authors consider that these results will clarify the present confusion in the literature concerned with the effect of the thyroid gland on antibody production, as different workers have used different animal species exclusively for their experiments. [See also this *Bulletin*, 1956, v. 31, 472; 1957, v. 32, 295.]

Elizabeth M. Harper

MAKINODAN, T., FRIEDBERG, Betsy H., TOLBERT, M. G. & GENGOZIAN, N. **Relation of *Secondary* Antigen Injection to Time of Irradiation on Antibody Production in Mice.** *J. Immunology.* 1959, Aug., v. 83, No. 2, 184–8, 3 figs. [13 refs.]

SCHWARTZ, R., EISNER, Anna & DAMESHEK, W. **The Effect of 6-Mercaptopurine on Primary and Secondary Immune Responses.** *J. Clin. Investigation.* 1959, Aug., v. 38, No. 8, 1394–403, 7 figs. [40 refs.]

"1. The administration of 6-mercaptopurine (6-MP), a purine analog, to rabbits in a dosage of 6mg. per Kg. per day resulted in complete blocking of the primary immune responses to a soluble protein antigen.

"2. Below the dose of 6mg. per Kg. per day a linear relationship was found to exist between the effect on the primary response and the dose of the drug.

"3. That dose of 6-MP which completely blocked the appearance of the primary response was only partially effective in preventing the onset of the secondary response."

DIXON, F. J. & WEIGLE, W. O. **The Nature of the Immunologic Inadequacy of Neonatal Rabbits. II. Antibody Formation by Neonatal Splenic Cells transferred to Adult Recipients.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 139–46. [15 refs.]

The authors have previously shown [this *Bulletin*, 1957, v. 32, 819] that adult rabbit lymphoid cells which have been sensitized with antigen will readily form antibody when transfused into irradiated adult rabbits but produce very little when injected into neonatal rabbits. They now report experiments to determine if neonatal lymphoid cells will produce more antibody if removed from the neonatal rabbit.

Cell suspensions were made from the excised spleens of 9 rabbits aged from 4 to 14 days. Each suspension was treated for 30 minutes at 37°C. with a soluble extract of *Shigella flexneri* 3, and injections of treated suspensions were made subcutaneously into 32 neonatal rabbits and 46 adult rabbits which had received 400 r of X-radiation 2 days before. Adults were given larger doses of cell suspensions than neonates but in terms of dosage per unit of body weight the neonatal rabbits received 4 times as much as the adults. The geometric means of agglutination titres for *Sh. flexneri* 3 of the sera of rabbits in each group were 9 for the neonates and 146 for the adults.

A second series of experiments is reported which confirms the work described in the earlier paper referred to above. After injection of antigen into the foot pads of adult rabbits, tissue from their lymph nodes was transferred to 120 neonatal rabbits and 62 irradiated adults. Geometric mean agglutination titres were 22 for the young animals and 561 for the adults.

The failure of neonatal rabbits to produce antibody

appears to be due to some other cause than the lack in the new-born animals of cells capable of antibody formation. *I. B. R. Duncan*

TALMAGE, D. W. **Immunological Specificity. Unique Combinations of Selected Natural Globulins provide an Alternative to the Classical Concept.** *Science.* 1959, June 19, v. 129, 1643–8, 2 figs. [35 refs.]

It is believed that antibodies must be different and unique for each of the many antigenic substances to which a distinctive immune response may be elicited. In a detailed argument the author concludes that such a hypothesis is unnecessarily complex and it is suggested that as an alternative to a unique antibody for each distinct antigen one may postulate a combination of naturally-occurring globulin molecules which is unique for each antigen.

In the terms of the hypothesis, a single globulin may combine with many different antigens but in a mixture of a large number of different globulins, the dominant activity will be that which is common to the largest number of globulin molecules in the mixture. It is argued that the specificity of an antiserum containing a mixture of different globulins is likely to be much higher than that of an antiserum containing only one species of globulin molecule. The presence of a multiplicity of globulins reduces the required concentration of each individual type so that the concentration reacting by chance with an unrelated antigen is below the detection threshold. However, a structurally related antigen reacting with a sufficiently high percentage of the globulins present may exceed this threshold and give cross reaction. The implications of the hypothesis are discussed. [The hypothesis is an extension of the clonal selection theory, though this is not mentioned in the paper. The probability of steric hindrance occurring in the course of the combination of several globulin molecules with a single antigenic determinant would appear to be quite high but the author does not consider this possible objection.] *Max Sussman*

BJORNEBOE, M. & SCHWARTZ, M. **Investigations concerning the Changes in Serum Proteins during Immunization. The Cause of Hypoalbuminemia with High Gamma Globulin Values.** *J. Exper. Med.* 1959, Aug. 1, v. 110, No. 2, 259–70, 5 figs. [11 refs.]

"On hyperimmunization of rabbits with pneumococcal vaccine, increase in the content of gamma globulin and fall of albumin in the serum are produced. In such hyperimmunized rabbits, investigations of the plasma volume, albumin degradation, and the distribution of the albumin intra- and extravascularly were undertaken by Sterling's method employing rabbit albumin labelled with I^{131}.

"The investigations do not suggest any significant alteration in the albumin degradation nor in the distribution between the intra- and extravascular albumin. It was demonstrated that the plasma volume increases simultaneously with increase in the gamma globulin and fall in albumin.

"It is concluded that the fall in serum albumin observed is due to a regulative mechanism which attempts to maintain the colloid-osmotic pressure by increasing the plasma volume."

TAYLOR, A. B. & LEON, M. A. **Third Component of Human Complement: Resolution into Two Factors and Demonstration of a New Reaction Intermediate.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 587–8, 1 fig. [12 refs.]

"Human C'3 has been resolved into 2 factors, C'_a and C'_b. These factors acted in the order C'_a, C'_b, in the conversion of $EAhuC'_A$ to E. Formation and decay of a new intermediate complex between sensitized erythrocytes and human complement, $EAhuC'_B$ has been demonstrated."

TURK, J. L. **The Immune-Adherence Activity of Normal Serum.** *Brit. J. Exper. Path.* 1959, Apr., v. 40, No. 2, 97–106, 1 fig. [12 refs.]

The immune-adherence phenomenon described by NELSON [this *Bulletin*, 1954, v. 29, 1189], in which an antigen, after coating with its specific antibody and fixing all 4 components of complement, is found to adhere to primate red cells, was used to investigate the immunological activity of a variety of normal sera to certain particulate antigens. These included starch grains and the cells of a number of bacterial species. Immune-adherence activity of normal guineapig, adult rabbit and human sera and of the sera of young calves and young rabbits was determined by finding the greatest dilution of serum which would cause adherence of antigen particles to at least 20% of human red cells added to a mixture of antigen, serum and complement.

Immune-adherence was found to occur with normal guineapig, rabbit and human sera against starch, *Salmonella typhi, Shigella flexneri, Escherichia coli, Vibrio el tor, Staphylococcus aureus* and *Erysipelothrix rhusiopathiae.* It appeared to be due mainly to a non-specific activity associated with the euglobulin fraction of the serum. This non-specific activity was absorbed by a wide range of bacteria and polysaccharides and had many properties in common with properdin [see PILLEMER, *ibid.*, 1955, v. 30, 83]. The specific activity in most sera tested made only a minor contribution to immune-adherence, but there were exceptions to this finding. For example, rabbit sera against starch and guineapig sera against *E. rhusiopathiae* showed much higher specific than non-specific activities. The specific activity was associated with the pseudo-globulin fraction of serum and appeared to be attributable to the presence of specific antibody.

Newborn calves showed non-specific immune-adherence and no specific activity, whereas newborn rabbits had high specific and no non-specific activity. This difference is presumably the result of the transfer of antibodies from the maternal circulation to the foetus in the rabbit but not in the cow.

Immunization of a rabbit with *Salm. typhi* led to a long-lasting increase in specific activity against *Salm.*

typhi and a short-term increase in non-specific activity against other bacterial species. [These results indicate that the demonstration of immune-adherence activity in a serum does not necessarily imply the presence of specific antibodies in that serum.] *R. B. Morrison*

BIER, O. G. & SIQUEIRA, Maria. **Prevention by Intravenous Injection of Antigen and Antibody of Passive Arthus Reaction to Unrelated Immune System.** *Proc. Soc. Exper. Biol. & Med.* 1959, July, v. 101, No. 3, 502–5, 1 fig. [10 refs.]

"1. Previous intravenous injection of antigen and antibody prevents development of passive Arthus reaction to an unrelated immune system in guinea pigs. 2. This suppressive effect does not seem to depend on C' depletion but rather on deficiency of platelets in circulating blood."

BENACERRAF, B., SEBESTYEN, Martha M. & SCHLOSSMAN, S. **A Quantitative Study of the Kinetics of Blood Clearance of P^{32}-Labelled *Escherichia coli* and Staphylococci by the Reticulo - Endothelial System.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 27–48, 8 figs. [35 refs.]

Escherichia coli and *Staph. aureus* labelled with ^{32}P were injected intravenously into a variety of animals, and the response of the reticulo-endothelial system (RES) under different experimental conditions was studied.

The findings were as follows:

When moderate numbers of organisms were injected the blood was rapidly cleared, and the clearance rate bore an exponential relationship to time for 90% of the injected dose. When the dose was very large, however, the RES became overloaded, and the blood clearance time was prolonged.

The rabbit cleared *E. coli* 30 times as rapidly as the mouse; this is probably correlated with the rabbit's much higher concentration of natural *E. coli* antibody. Mice passively immunized with *E. coli* antibody showed enhanced clearance times compared to normal mice for this organism. *E. coli* incubated with its antibody *in vitro* before injection was cleared more rapidly by normal mice than the same organism not so treated. On the other hand the mouse, which has a high natural antibody to *Staph. aureus*, cleared this organism with such rapidity that it was found impossible to increase the rate by passive immunization.

The authors demonstrated that the liver was a more important site than the spleen for phagocytosis of *E. coli* in the rabbit and the mouse, especially when the organisms were well opsonized (high serum antibody). With poorly opsonized bacteria the proportion dealt with by the spleen increased, since the sluggish circulation in this organ allowed more intimate and prolonged contact between the RE cells and bacteria.

Mice previously treated with endotoxins from a variety of Gram-negative bacteria phagocytosed *E. coli* more rapidly than normal mice. This is attributed to mechanisms of cross-immunity and not to any consequential increase in the phagocytic powers of the RES. The elements in the RES which deal with bacteria are the same as those that deal with injected inert colloids.

The authors stress the importance of the role of specific antibody in facilitating phagocytosis of bacteria by the RES, and find a close identity between the reactions of the RES to bacteria and inert colloidal particles.

Heat-killed bacteria were used in these experiments, since the RES behaves towards them in the same way as it does to living bacteria. If virulent strains are used, there is often a secondary bacteriaemia after the initial clearance, and this may be lethal. *J. H. McKay*

BENACERRAF, B., KIVY-ROSENBERG, Evelyn, SEBESTYEN, Martha M. & ZWEIFACH, B. W. **The Effect of High Doses of X-Irradiation on the Phagocytic, Proliferative, and Metabolic Properties of the Reticulo-Endothelial System.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 49–64, 3 figs. [31 refs.]

Rats and mice were subjected to X-irradiation and the effect of this on the function of the reticulo-endothelial system (RES) was studied.

After LD50 dosage neither species was inferior to normal controls in the ability to phagocytose colloidal carbon, but mice receiving a lethal dosage showed a fall in this function before death. Control rats, after RE blockade with colloidal carbon, recovered normal RE function by the fourth day; but irradiated rats (LD50) showed a delay.

Zymosan, which can increase phagocytic activity tenfold in mice (due to its proliferative action on RE tissue) was found inactive in previously irradiated animals. Irradiated mice cleared injected *Escherichia coli* as rapidly as normal controls, presumably because both have the same level of serum antibody. Immunized irradiated mice, however, cleared this organism at a slower rate than non-irradiated immunized controls. This was thought to be due to the failure of the immunized irradiated mice to produce extra antibody, on which rate of phagocytosis largely depends. The concentrations of hepatic enzymes concerned in the catabolism of denatured albumin were not reduced after LD50 irradiation in mice.

Discussing their results the authors concluded that the increased susceptibility to infection which follows irradiation is largely due to depression of antibody formation and inability of the irradiated RES to proliferate in response to the stimulus of infections.

J. H. McKay

Miscellaneous

DÖLL, H. Die Hygiene des Friseurgewerbes in Berlin. [**Hygiene of Hairdressing Establishments in Berlin**] *Städtehyg.* 1959, Aug., v. 10, No. 8, 155–7.

In Berlin official regulations in respect of hygiene in hairdressing establishments are in force both in the Western and Eastern sectors. The author of the present paper describes some of the existing conditions which contravene these regulations and makes certain recommendations for additions to these regulations. Among the defects in hygiene which the author describes in some detail are:—(1) bad ventilation and lighting, (2) lack of general cleanliness, (3) personal hygiene is often most unsatisfactory—hair dressers should always be clean, wash their hands carefully between customers and not smoke while working, (4) the cleanliness of overalls for attendants and customers is often doubtful, (5) the technique of shaving is in many respects unhygienic as for example in the absence of adequate disinfection of shaving brushes between customers and the practice of barbers to rub in the lather by hand, and (6) the very imperfect cleansing and disinfection of the implements and apparatus after use.

Some of the imperfections of the present regulations are discussed. Stress is laid on the particular need for the supervision of hairdressing establishments in hospitals, railway stations, ports, airports and holiday resorts. *M. E. Delafield*

Book Reviews

BURNET, Macfarlane [O.M., F.R.S.]. **The Clonal Selection Theory of Acquired Immunity.** pp. ix+209, illustrated. 1959. Nashville: Vanderbilt University Press, Tennessee, U.S.A. London: Cambridge University Press, Bentley House, 200, Euston Road, N.W.1. [22s. 6d.]

This book is a record of the Abraham Flexner Lectures of Vanderbilt University, given by the author in 1958. The theme is the ecological and evolutionary implications of the clone, as contrasted with the sexually reproducing population. This theme is developed in many fields of microbiology, and perhaps the most interesting part is that which deals with antibody production.

In 1949, BURNET and FENNER wrote a book called *Production of Antibodies* [this *Bulletin*, 1950, v. 25, 1081] in which they described an indirect template theory of antibody production, in opposition to the HAUROWITZ-PAULING direct template theory. The indirect template theory postulated that antibody production could continue long after the effective antigen had disappeared from the body because a genocopy of the antigenic determinant was incorporated in the genome of the stem cell, allowing the indefinite production of descendent antibody-producing cells.

The evidence which seemed to discredit the direct template theory by showing that antibody production could continue after the disappearance of all the effective antigen has never seemed really decisive. Although 99% of an antigen may have disappeared, the remaining 1% may still represent a large number of molecules.

However, the really unsatisfactory part of the indirect template theory was the additional postulate to account for the non-antigenicity of body components: these were assumed to carry "self-markers" and, in addition, the antibody-producing cells were supposed to have a "recognition unit" to act as a means of detecting material carrying self-markers. Since no mechanism for recognition was suggested, the theory was little more than a re-statement of the original problem.

However, Sir Macfarlane has never been slow to abandon a theory when a better one appeared, and in these lectures he argues, with equal enthusiasm, for the clonal selection theory of antibody production. The idea was suggested by JERNE in 1955 (*Proc. Nat. Acad. Sci., Wash.*, 1955, v. 41, 849) and it is supposed that many clones of globulin-producing cells exist, each responsible for one genetically determined type of antibody globulin. The theory postulates that an antigen does not specifically induce the production of an antibody complementary to it, but rather that there pre-exist clones of cells which are producing globulin with sites complementary to any possible antigenic determinant.

When an antigen is introduced, it will make contact with a cell of the appropriate clone because the globulin complementary to it is on the surface of the cells of the clone. The theory postulates that this union at the surface stimulates the production of more globulin of this type by initiating proliferation of the cells, and thus enlargement of this particular clone.

To account for the non-antigenicity of body components, it is now suggested that, at some point in embryonic life, all clones which were capable of reacting with determinants on body components were eliminated; this elimination is supposed to be due to the death of the cells which combine with antigens, so that the effect on the cells is the opposite of that which occurs in adult life.

The implications of the new theory are discussed in relation to a number of infective and neoplastic diseases.

[The reader of this stimulating volume may be interested to study also two recent papers which have appeared in *Science*. In one of these papers, [see above p. 1308], D. W. TALMAGE argues that, with a

moderate number of pre-existing globulin types, it is possible to account for all the antigenic specificity which, until recently, seemed to demand some kind of template theory for antibody production.

In the other paper, [see above p. 1306] Joshua LEDERBERG considers the theory that the information required to synthesize a given antibody is already inherent in the organism before the antigenic stimulus is received; the antigen stimulates that mechanism electively. He states 9 propositions which, if they could all be shown to be true, would provide a solid basis for an elective theory.] *Forrest Fulton*

BROCKINGTON, C. Fraser. **World Health.** 405 pp., illustrated. 1958. [A425 Pelican Med. Ser.] Harmondsworth: Penguin Books Ltd., Middx. [5s.].

In creating the World Health Organization, the United Nations gave two new conceptions to the world: the first, that health is a positive state—"a state of complete physical, mental and social well-being"—rather than a mere temporary freedom from disease; the second, that all the problems of health, not only those of a few communicable diseases, should be considered in global terms. Many people who applauded the first may never have given a thought to the second, perhaps justifiably since the reasoning behind it was clear only to a few highly professional individuals. Professor Brockington has now expounded it at length. His argument is developed lucidly, making full use of encyclopaedic scholarship and a comprehensive knowledge of the literature. Every aspect of the problems of world health, geography, population, social habit, economic development, urbanization, food and so on, and the work of national health services and of the World Health Organization, is placed in perspective. There is not a single example of obscure medical jargon throughout. The result is a book which anyone interested in humanity will find of absorbing interest, and which (as the editorial foreword states) should be read by all students of medicine, social workers, colonial administrators and internationally minded politicians. The reviewer would go further and recommend it strongly as a standard textbook for medical students and postgraduate students of tropical medicine and public health. To any public health worker, the list of references alone would be worth the modest purchase price of the book. Nothing like it has been written before, and its appearance emphasizes the need for such a work. *B. B. Waddy*

PATTY, Frank A. [Edited by.] **Industrial Hygiene and Toxicology.** 2nd Revised Edition. Vol. I. **General Principles.** pp. xxviii+830, numerous figs. 1958. New York 1: Interscience Publishers, 250, Fifth Avenue, N.Y. London: 88/90, Chancery Lane, W.C.2. [£6. 12. 0.]

After a period of 10 years, Mr. Patty and his collaborators have undertaken the revision of *Industrial Hygiene and Toxicology* [this *Bulletin*, 1949, v. 24, 1024] and because the subject has expanded so rapidly during the intervening years the new edition will encompass 3 volumes instead of 2. Volume I is named *General Principles,* Volume II will be entitled *Toxicology* and Volume III *Industrial Environmental Analysis.* Certain sections in Volume I have been rearranged and the changes are consistent with the trends in thought and practice during the post-war period. More space and emphasis is now given to noise, heat, ionizing radiation, human engineering and industrial safety, sanitation, air pollution and illumination.

In his preface to the first edition, Mr. Patty defines industrial hygiene as "the science and art of preserving health through the recognition, evaluation, and control of environmental causes and sources of illness in industry." And then he continues "It resolves itself into the problem of finding factors or conditions in workplaces that may cause or contribute to the illness or serious discomfort of employees, and of devising methods and means of eliminating or controlling such conditions". This philosophy permeates the theme of Volume I and is supported by all the authors, for much of the subject-matter in all the chapters relates to the provision of "comfortable" or "physiologically correct" working conditions rather than to the correction of environmental faults leading to overt industrial disease.

With few exceptions, clarity and simplicity of style have been achieved without a reduction of technical or scientific accuracy and there is much common sense and practical guidance to be found in all the contributions. No person actively practising industrial hygiene should omit to read the chapters Industrial Hygiene Records and Reports and The Industrial Hygiene Survey and Personnel by Ruth and Frank PATTY respectively. The monograph by Ross A. MCFARLAND on a difficult and esoteric subject, Human Engineering and Industrial Safety, is outstanding, which is fortunate, for the thesis is so neglected in modern industry, and yet if given attention would result in a tremendous increase in human well-being and efficiency. It is an invidious task to select the highlights in a publication which attains such a consistently high standard, but the sections on Ventilation, Explosion and Fire Hazards of Combustible Dusts, Physiological Effects of Abnormal Atmospheric Pressure and Lighting for Seeing are particularly good; the discussions on air-sampling techniques, permissible limits and food handling are stimulating.

How often, outside the U.S.A., is Frank Patty's first rule for an industrial hygienist adopted, *viz.*: "The first rule the industrial hygienist should adopt regarding analytical methods is never to rely upon a method until he has personally tried it out under controlled conditions, such as (1) by sampling a synthetic atmosphere from a proportioning apparatus or from a gastight, impervious chamber of sufficient size to permit making and sampling mixtures without introducing significant errors . . ."? The reviewer would like to have seen more discussion on the characteristics and merits or otherwise of dust sampling instruments and methods of dust analysis, and on the aetiology of silicosis. Professor T. F. HATCH seems to have been rather too concise and mathematical in his section on Heat Control in the Hot Industries.

The book is printed in legible type, the illustrations are clear, and there are many references which are advantageously situated at the bottom of the page. The main criticism from the individual subscriber must be one of price, but the content of the book has not been overvalued.

Any industrial hygienist, or industrial physician practising industrial hygiene, who is foolhardy enough to omit "Patty" from his library will live to rue the day. The first edition of Volumes I and II was unique and invaluable, and the new edition of Volume I has lost none of its pre-eminence. The reviewer looks forward impatiently to the arrival of Volumes II and III.

P. J. R. Challen

GALE, A. H. **Epidemic Diseases.** 159 pp., 21 figs. 1959. [A456 Pelican Med. Ser.] Harmondsworth: Penguin Books Ltd., Middx. [3s. 6d.]

This little book fulfils admirably its purpose of giving to the layman—and others—a picture of the history of the common infectious diseases which have been epidemic in Britain at times in the period from about the 14th century to the present day. It is easy to read, written in simple and non-technical words wherever possible, but is never dull. There is a bibliography of 63 items which have been chosen with discrimination. But the book is not merely a compilation, for the author draws on his own experience as an epidemiologist. An examination of the sources of information from the monastic histories and state documents of the earliest period, the later Bills of Mortality up to the present day of registered vital statistics precedes the chapters on infectious diseases. These are on plague, influenza; leprosy, syphilis and smallpox; cholera; continued fevers; summer diarrhoea; throat distempers—scarlet fever and diphtheria; measles and whooping-cough; epidemic diseases of the central nervous system; malaria and yellow fever; and tuberculosis. The causation of each disease is described shortly and its history told with an account of the gradual changes in medical opinion resulting from advances in scientific knowledge and methods of control, the evidence of more precise statistical data and improvements in the techniques of epidemiological investigations.

The final chapter contains an analysis and discussion of the relative importance of the different diseases at different times.

M. E. Delafield

MORICHAU-BEAUCHANT, Jacques. La santé dans le monde. [**Health throughout the World**] 126 pp. 1958. Paris: Presses Universitaires de France, 108, Boulevard Saint-Germain.

This booklet, No. 782 in the series entitled "Que sais-je?", was compiled with the purpose of presenting a picture of the state of health of the different parts of the world not merely from the medical point of view but from the more important angle of the extent of the development of a country in respect of the economic, social and cultural level to which it has attained. The author has succeeded admirably in this purpose for the material is chosen with discrimination and the presentation of it is clear, balanced and most readable.

In the 123 pages of the booklet there are 7 chapters which cover statistics, the evolution of health in Europe, health in under-developed countries, the dangers of overpopulation, the effects of improved health of the people, public health programmes and public health in relation to human problems. The shortest chapter is on statistics but gives enough information on comparative mortality and morbidity to indicate the differences between countries of the world and the changes which have occurred in the passage of time. The longest chapter is on the under-developed countries and in it the many factors influencing the state of health in these countries are simply but effectively stated. The booklet though so small contains much information which is also discussed by the author. It should be of interest not only to laymen but to all concerned with the health of peoples.

M. E. Delafield

Printed in Great Britain by The Eastern Press, Ltd., London and Reading